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ORIGINAL RESEARCH

Prevalence and predictors of depression in patients with systemic lupus erythematosus: a cross-sectional study

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Objective: The purpose of this study was to estimate the prevalence and examine the predictors of depression in patients with systemic lupus erythematosus (SLE).

Methods: This cross-sectional study was conducted in the rheumatology clinic of a university hospital. All SLE patients that met the revised American College of Rheumatology (ACR) classification were included in the study. Sociodemographic data and medications were recorded. Disease activity for SLE was assessed with the Mexican-SLE Disease Activity Index (Mex-SLEDAI). All subjects were screened for anxiety and depression by using the Hamilton Anxiety Rating Scale (HAM-A) and the 17-item version of the Hamilton Depression Rating Scale (HAM-D17). Multiple linear regression analyses were used to determine predictors of depressive disorder.

Results: A total of 62 SLE (61 females and 1 male) patients participated in the study. Based on HAM-D17 and HAM-A, rates of depression and anxiety in SLE patients were 45.2% and 37.1%, respectively. The multiple linear regression analysis revealed that HAM-A score and younger age were significant predictors of depression in SLE patients.

Conclusion: The findings suggest that depression and anxiety are common in SLE patients. In addition, higher levels of anxiety and a younger age may increase the risk of depression. Because of the small sample size, further studies should be conducted to confirm these results.

Keywords: systemic lupus erythematosus, depression, anxiety disorder

Introduction

Depression is common in the general population. A meta-analysis of data obtained from several countries showed that 1-year and lifetime prevalence rates of major depressive disorder (MDD) were 4% and 7% respectively.[1] A higher prevalence rate of depression is found in patients with a chronic medical illness. Recently, a study of patients with systemic sclerosis showed that 1-year and lifetime prevalence rates of MDD were 11% and 23% respectively.[2] Those rates are approximately twice that of the general population.[2] Similarly, recent evidence suggests that the prevalence of depression in cancer patients is as high as 30% and depressive severity is associated with severity of physical pain.[3]

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease which usually affects multiple organ systems including the central nervous system.[4,5] Therefore, it can cause several neuropsychiatric syndromes, including depression.[6,7] Recent evidence suggests that the prevalence of depression in SLE patients is between 11.5% and 47%.[8–13] In addition, a recent study suggests that severity of depression increases with more severe disease activity of SLE.[14] The extended life span of SLE patients from

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current advances in medicine leads these patients to encounter a relapsing and remitting course of the disease and adverse events from several treatments that may deteriorate their quality of life and intimate relationships, and may precipitate depression.[15,16] In addition, the burden of SLE comorbid with depression may increase the risk of suicide.[17]

Although awareness of psychiatric complications has increased among physicians and other health professionals, little research focuses on depressive aspects of SLE. Therefore, the aim of the current study was to determine the prevalence of depressive disorders in SLE patients and to identify risk factors.

Material and methods

Patients

The study used the clinical data from the cross-sectional SLE study. Patients were recruited from the Rheumatology Clinic of University Hospital, Chiang Mai University, Thailand.[18] All SLE patients, aged 18–60 years, fulfilling the inclusion criteria for their diagnosis based on the revised American College of Rheumatology (ACR) classification[19] were included in this study. Exclusion criteria included unstable medical conditions, impaired consciousness, a significant hearing impairment, any degree of visual impairment, or lack of the necessary communication skills to ensure the reliability of test scores. The study was approved by the Medical Ethical Committee of Chiang Mai University, and all subjects gave an informed consent.

Evaluation

Clinical characteristics

The rheumatologist (WL) reviewed a series of interviews, demographic data, and all medical records; did physical examinations and monitored laboratory tests (complete blood count, erythrocyte sedimentation rate, urinalysis, liver function tests, and serum creatinine). The history of central nervous system (CNS) involvement such as a history of seizures and any episode of delirium was also noted. The Mexican-SLE Disease Activity Index (Mex-SLEDAI), a standardized index derived from clinical and serological variables,[20] was used to assess disease activity twice (firstly at the time of SLE diagnosis and later on screening for study inclusion).

Assessment of depressive and anxiety disorders

The psychiatrists evaluated for levels of anxiety and depression in all patients using the 17-item version of the Hamilton Depression Rating Scale (HAM-D17)[21] and the Hamilton Anxiety Rating Scale (HAM-A).[22] Based on the HAM-D17, depression is defined as scores equal to 11 or more.[21,23] Cut-off scores for anxiety, as measured by the HAM-A, are as follows: 0–13 no anxiety, 14–17 mild anxiety, 18–24 moderate anxiety, and 25–30 severe anxiety.[22]

Statistical analysis

Descriptive analysis of sociodemographic data and clinical variables were undertaken. The dependent variable in the present study was depression. The Student's *t*-test and Mann–Whitney *U*-test (for continuous variables), and the Fisher's exact test and a Chi-squared test (for categorical variables) were used to examine the significant association (contingency) of independent variables between the depressive and nondepressive groups. Multivariate analysis was performed by using the linear regression model. Each independent factor which was statistically significant at the bivariate level ($P < 0.1$) was included in the analysis. We then developed a final model that combined patient characteristics, considering inclusion variables independently associated with depressive disorder in the SLE patients. All data were analyzed by using the SPSS (version 17; SPSS Inc, Chicago, IL, USA).

Results

The 62 SLE patients (female vs male, 61:1) were included in this analysis. Mean age ± standard deviation (SD) of those patients was 31.8 ± 9.0 years. Of those, 33.9% of them had completed 13 years of education, while the rate of unemployment was 40.3%. Mean ± SD disease duration of total patients was 73.7 ± 57.8 months. Mean ± SD of the HAM-A and HAM-D17 scores of those patients were 12.4 ± 9.4 and 10.6 ± 8.8 respectively. Based on HAM-A score, 37.1% of the patients had an anxiety disorder. Of all anxious patients, 30.4%, 34.8%, and 34.8% of them had severe, moderate, and mild anxiety, respectively. Disease activity indices at the first time of SLE diagnosis and at the time of interview were 13.1 ± 5.2 and 3.5 ± 3.7, respectively. Forty-five percent of total patients experienced CNS involvement, frequently receiving various medications to treat SLE at any potential time point in the course of their illness, including prednisolone, methotrexate, chloroquine, or cyclophosphamide.

Based on the HAM-D17 score, 45.2% of the patients were defined in the depressive group. Table 1 compares the clinical characteristics between depressive and non-depressive groups of the SLE patients. Comparison of the two groups, by sex, education duration, disease duration, disease activity and current medications showed no significant differences. In addition, several medications, administered for SLE treatment, were not significantly different in the two groups in terms of number, type, duration and dose (see Table 2). Significant differences

Table 1 Characteristics of SLE patients

	SLE without depression (n = 34)	SLE with depression (n = 28)	*P*-value
Age	33.7 ± 8.9	29.6 ± 8.7	0.076
Gender: female	34 (100%)	27 (96.4%)	0.452
Education			0.638
Less than 6 years	0 (0%)	1 (3.6%)	
At least 6 years	8 (23.5%)	5 (17.9%)	
7–9 years	3 (8.8%)	5 (17.9%)	
10–12 years	10 (29.4%)	9 (32.1%)	
13 years or more	13 (38.2%)	8 (28.6%)	
Unemployment	8 (23.5%)	17 (60.7%)	0.003*
Disease duration (months)	85.0 ± 63.9	60.0 ± 46.9	0.134
HAM-A total score (mean ± standard deviation)	6.1 ± 3.5	20.1 ± 8.7	<0.001*
HAM-D17 total score (mean ± standard deviation)	3.8 ± 2.7	18.9 ± 6.2	<0.001*
Disease activity at the time of SLE diagnosis	12.7 ± 5.0	13.6 ± 5.4	0.482
Current disease activity at the time of psychiatric assessment	3.0 ± 3.3	4.1 ± 4.1	0.255
History of CNS involvement	12 (35.3 %)	16 (57.1 %)	0.085
Current medications for SLE treatment			0.573
One	12 (35.3%)	8 (28.6%)	
More than one	22 (64.7%)	20 (71.4%)	
Lifetime medications for SLE treatment			0.096
One	4 (11.8%)	8 (28.6%)	
More than one	30 (88.2%)	20 (71.4%)	

Abbreviations: CNS, central nervous system; HAM-A, Hamilton Anxiety Rating scale; HAM-D17, 17-item Hamilton Depression Rating Scale; SLE, systemic lupus erythematosus.
Note: *Significant difference ($P < 0.05$).

($P < 0.05$) were found among the two groups in the HAM-A score ($P < 0.001$) and unemployment ($P = 0.003$). As a result, these factors were included in multiple linear regression analysis as independent variables. Moreover, other factors which had significant differences ($P < 0.1$) were also included in the analyses (age, history of CNS involvement and a number of lifetime medications). The findings suggest that depression severity are significantly associated with the HAM-A and age (adjusted R square = 0.799, Durbin-Watson = 1.796) (see Table 3).

Discussion

This study suggests that the prevalence of depression and anxiety in SLE patients is high. The point prevalence of depressive and anxiety disorders in SLE patients are 45.2%

Table 2 Mean doses of each drug treatment for SLE patients with/without depression

Drugs	SLE without depression	SLE with depression	*P*-value
	Mean ± standard deviation	Mean ± standard deviation	
Current dose of prednisolone (mg/day)	13.6 ± 12.7 (n = 34)	14.5 ± 13.0 (n = 28)	0.547
Lifetime dose of prednisolone (g)	15.7 ± 12.3 (n = 34)	12.2 ± 9.4 (n = 28)	0.273
Current dose of methotrexate (mg/day)	5.0 ± 0.0 (n = 2)	7.5 ± 0.0 (n = 1)	0.157
Lifetime dose of methotrexate (g)	220.0 ± 56.6 (n = 2)	323.8 ± 83.1 (n = 2)	0.121
Current dose of chloroquine (mg/day)	211.1 ± 51.6 (n = 18)	217.9 ± 45.4 (n = 14)	0.799
Lifetime dose of chloroquine (g)	147.4 ± 103.1 (n = 23)	157.5 ± 101.3 (n = 14)	0.234
Current dose of cyclophosphamide (mg/day)	50.0 ± 0.0 (n = 10)	50.0 ± 0.0 (n = 10)	1.000
Lifetime dose of cyclophosphamide (g)	20.6 ± 19.5 (n = 15)	13.9 ± 12.3 (n = 11)	0.337

Abbreviation: SLE, systemic lupus erythematosus.

Table 3 Multiple linear regression analysis of predictors for depressive disorder in SLE patients

Variables	Multiple linear regression coefficient (β)	SE (β)	*P*-value	95.0% CI of OR
HAM-A	0.826	0.054	<0.001	0.718 to 0.933
Age	–0.164	0.057	0.05	–0.277 to –0.051
Constant	5.537	1.993	0.007	1.55 to 9.53

Abbreviations: HAM-A, Hamilton Anxiety Rating scale; 95% CI, 95% confidence interval; OR, odds ratio; SE, standard error; SLE, systemic lupus erythematosus.

and 37.1%, respectively. Depression severity is associated with higher anxiety and younger age.

In general, prevalence of psychiatric manifestations is high in the SLE patients.[6,24,25] Of those, depression is one of the most common mental illnesses.[26] Similar to present findings, the recent studies suggest that the point prevalence of depressive disorder in SLE is up to 39%,[27] while the lifetime prevalence is up to 69%,[28,29] which is far more prevalent than that of the general population in which the point and lifetime prevalence is 6.1% and 10.3%, respectively.[1] The high morbidity of depression in SLE warrants continuing research and expansion of efforts in the clinical setting to optimize treatments.

Compared with the general population, anxiety is another common psychiatric manifestation in SLE populations. A recent study found that the 30 day and lifetime prevalence for anxiety in SLE patients, including agoraphobia without panic disorder, generalized anxiety disorder and other anxiety disorder, were 46.5% and 52.1%, respectively.[28] Similarly, another group found that the prevalence of anxiety, as measured by the HAM-A, was as high as 65.7%.[30] Because of the high prevalence of anxiety, individual SLE patients should undergo psychiatric assessment for anxiety.

In general, the relationship between depression and anxiety in patients across different ages with chronic somatic disease has been reported. Recently, the evidence suggests that the anxiety trait is a significant determinant of depressive symptoms in patients with breast cancer.[31] The recent study of patients with pain symptoms also suggests that anxiety and depression may correlate positively.[32] In addition, the significant relationship between them has been reported in the advanced cancer patients with median age of 59 years (range 20–91 years).[33] Like the present findings, the relationship between both anxiety and depression in SLE patients was also noted in the previous study.[34] Thus, all patients with chronic medical illness, including SLE patients, should be also evaluated for depression and anxiety.

Based on these findings, a younger age of patients with SLE is also associated with depression. Similarly, it was previously found that in pediatric inpatients with SLE there was a higher prevalence of major depressive disorder.[35] Those with early onset SLE may also have difficulties in living with SLE-related disability. Long-term distress in adjusting to their lives with disability may play a role in causing depression. For anxiety, it is a symptom commonly found in depressed patients. In any event, depressive and anxious functional brain pathology has substantial overlap in their functional correlates and might be part of the same process. Therefore, screening for anxiety in SLE younger patients may be beneficial in term of evaluation and management.

Disease activity indicating severity of SLE relates to depression. A study of 71 female patients with SLE found that disease activity was associated with depression severity measured by the Montgomery-Asberg Depression Rating Scale (MADRS).[36] Unfortunately, the findings from our study did not show this association between them. Reasons for these differing results are unclear. However, one possible explanation for the different findings is the potentially confounding influence of prednisolone, a medication which can induce depression.[37] Mean doses of prednisolone in a previous study were 18.28 mg/day for the major depressive disorder (MDD) group and 15.0 mg/day for the non-MDD group,[36] while mean doses of this medication in our study were less than that of a previous study.[36] Further research with a larger sample size and well-controlled study methodology may clarify these phenomena.

CNS involvements in SLE may be one of the major causes of morbidity and mortality. It is also associated with psychiatric manifestations, particularly in psychosis (23%).[38] A previous study in childhood SLE suggests that mood disorder is not a common neuropsychiatric manifestation in SLE patients with CNS involvement,[39] which is similar to present findings. So far, the explanation has been unclear, however, mood disorder in those patients, especially in depression, may come from several causes, including pathology in CNS or psychological reaction of the disease.

There are some limitations in this study. Firstly, the findings resulted from a small sample size, and therefore, it should be interpreted with caution. To confirm these analyses, a large sample size study should be conducted. Secondly, since there is high prevalence of SLE in women, nearly all participants in this study were female. Generalization from

this analysis to male SLE patients should be done cautiously. To balance the sex ratio in further studies may be beneficial to substantiate these findings. Finally, patients included in this study had medical complications caused by SLE and also took several medications, which may affect the prevalence of depression or anxiety. To apply those findings to other SLE populations should again be a matter for caution.

In summary, depression and anxiety are highly prevalent in SLE patients. Anxiety and young age are associated with depressive disorder in those patients. Therefore, routine screening for the predictors for those patients in clinical settings may be beneficial.

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Disclosure

The authors declare that they have no conflicts of interest in this work.

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