

Depression in Patients with Systemic Lupus Erythematosus: A Multicenter Study

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ABSTRACT

Background and Objective: Neuropsychiatric disorders including depression are common clinical manifestations of systemic lupus erythematosus (SLE). Depression in patients with SLE is under-recognized, although it is a treatable clinical entity. The present study aimed to determine the prevalence of depression and identify the relationship between depression and SLE disease characteristics.

Patients and Methods: This multicenter cross-sectional study was conducted in the rheumatology clinics of four tertiary referral hospitals in Saudi Arabia between April and September 2014. Patients' demographic data and SLE disease characteristics such as disease duration, severity and drug treatments were collected. A validated Arabic Beck Depression Inventory (BDI) score was used to estimate the prevalence of depression.

Results: A total of 68 patients with SLE (64 women, 4 men) were enrolled in the study. Forty-six (67.6%) patients were found to have BDI scores indicating depression; of them, only four patients (8.7%) were receiving antidepressant treatments. Higher prevalence of depression was associated with steroid treatment ($P = 0.046$).

Conclusions: The study results revealed high prevalence of depression among Saudi patients with SLE. Most of the study population were not adequately treated, suggesting inadequate recognition and treatment of depression in SLE.

Key words: Beck Depression Inventory, depression, Saudi, systemic lupus erythematosus

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, multisystem, autoimmune disorder that affects women (90%) more than men.^[1] SLE can involve almost all of the systems including the central nervous system and it can cause several neurological symptoms such as seizure, stroke, chorea, myelopathy and several psychiatric syndromes.^[2] During SLE, up to 75% of adult

patients suffer neuropsychiatric manifestations, which occur even when the disease is clinically and serologically quiescent.^[3,4] In SLE patients, the most common psychiatric disorder is depression.^[5] However, the prevalence of depression varies across populations from 17% to 75%.^[6-8] Mood disorders, including depression, were found to be associated with a lower health-related quality of life.^[4,9] It was also reported that depression

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could negatively affect treatment outcomes in the form of nonadherence to recommended treatments and clinic appointments.^[10] However, when treated promptly, mood disorders could be resolved in around 50% of patients with SLE.^[9] Therefore, recognition of depression and providing adequate treatment are important aspects of optimal management of SLE.

The aim of this multicenter cross-sectional study was to determine the prevalence of depression and identify the relationship between depression and disease characteristics in Saudi patients with SLE.

PATIENTS AND METHODS

Sixty-eight Saudi patients with SLE who attended Rheumatology Clinics at four tertiary referral hospitals in Saudi Arabia (King Fahad Medical City, Riyadh; Al Noor Specialist Hospital, Makkah; Security Forces Hospital, Riyadh, and King Abdulaziz Medical City, Riyadh) between

April and September 2014 were enrolled in the study. Inclusion criteria were Saudi nationality, aged ≥ 16 years fulfilling the American College of Rheumatology Revised Criteria for the Classification of SLE and willingness to give written informed consent [Table 1].^[11] Patients with unstable medical conditions, impaired consciousness, significant visual impairment or lack of necessary communication skills to ensure the reliability of test scores were excluded from the study.^[11] Data on demographic parameters, clinical features and treatments were collected and recorded. Laboratory evaluations included complete blood profile, urinalysis, anti-double stranded DNA antibodies, serum complements C3 and C4 and antiphospholipid (aPL) antibodies. Additionally, lupus anticoagulant, immunoglobulin (Ig) G, IgM, anticardiolipins and anti- $\beta 2$ -glycoprotein 1 were reviewed in all patients to evaluate any association with depression. Global disease activity was evaluated by SLE Disease Activity Index (SLEDAI). Accordingly,

Table 1: American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus

Criterion	Definition
Malar rash	Fixed erythema, flat or raised, over the malar eminence, tending to spare the nasolabial folds
Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation
Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by a physician
Arthritis	Nonerosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling or effusion
Serositis	Pleuritis; convincing history of pleuritic pain or rub heard by physician or evidence of pleural effusion OR Pericarditis; documented by electrocardiogram or rub or evidence of pericardial effusion
Renal disorder	Persistent proteinuria >500 mg/day or $>3+$ if quantitation not performed OR Cellular casts: May be red cell, hemoglobin, granular, tubular or mixed
Neurologic disorder	Seizures: In the absence of offending drugs or known metabolic derangement; e.g., uremia, ketoacidosis or electrolyte imbalance OR Psychosis: In the absence of offending drugs or known metabolic derangement; e.g., uremia, ketoacidosis or electrolyte imbalance
Hematologic disorder	Hemolytic anemia: With reticulocytosis OR Leukopenia: $<4000/\text{mm}^3$ total OR Lymphopenia: $<1500/\text{mm}^3$ on two or more occasions OR Thrombocytopenia: $<100,000/\text{mm}^3$ in the absence of offending drugs
Immunologic disorder	Anti-DNA: Antibody to native DNA in abnormal titer OR Anti-SM: Presence of antibody to SM nuclear antigen OR Positive finding of aPL antibodies based on An abnormal serum level of IgG or IgM anticardiolipin antibodies, A positive test result for lupus anticoagulant using a standard method OR A false-positive serologic test for syphilis known to be positive for at least 6 months and confirmed by <i>Treponema pallidum</i> immobilization or fluorescent treponemal antibody absorption test
ANA	Abnormal titer of ANA by immunofluorescence or equivalent assay at any point in time, in the absence of drugs known to be associated with drug-induced lupus syndrome

aPL – Antiphospholipid; ANA– Antinuclear antibody; Ig – Immunoglobulin

the patients were divided into five subsets (0: no activity; 1–5: mild activity; 6–10: moderate activity; 11–20: high activity and ≥ 20 : high activity). A validated Arabic Beck Depression Inventory (BDI) score was used to estimate the prevalence of depression and its severity.^[12] Scores for each category of BDI were interpreted as follows: 0–9: normal; 10–18: mild depression; 19–29: moderate depression and ≥ 30 : severe depression.^[12]

Ethical approval for this study (Protocol no.: HAPO-01-R-010) was provided by the Ethics Committee of King Abdulaziz City for Science and Technology (KACST), Riyadh, on May 4, 2015. Each patient gave written consent before study enrollment.

Data were analysed using SPSS software version 17.0 (SPSS Inc., IL, USA) by standard methods. Chi-square test or Fisher's exact test, whichever was appropriate, was used for comparison of categorical variables. Analysis of variance was utilized to compare the difference among continuous variables. A two-tailed $P < 0.05$ was considered as statistically significant.

RESULTS

All 68 patients completed the Arabic BDI. There were 64 women and 4 men with a median age of 30 years (age range: 16–59 years) and median disease duration of 5 years. Almost half of the patients (48.5%) were married, 38.2% had postsecondary education and 83.8% were not actively employed [Table 2]. Based on the Arabic BDI score, 67.6% of patients were found to have depression; of them, 33.8%, 20.6% and 13.2% had mild, moderate and severe depression, respectively. Only one patient (1.5%) had suicidal ideation, but no patient had any previous suicide attempt. Twenty-two patients (33.2%) had recent disease exacerbation within the previous year. Eighty-four percent of patients had active SLE (mild: 36.8%, moderate: 30.9%, high: 11.8% and very high: 4.4%). Fifty-six patients (82.4%) had received corticosteroid therapy with a median duration of 48 months and median dose of 5 mg/day. Forty-six (67.6%) patients had been subjected to immunosuppressive therapies. Almost 28% had positive aPL but only 16.2% had aPL syndrome (APS) [Table 3]. Of the 17 patients (25%) with comorbidities, 10 had hypertension as the major comorbid condition. Surprisingly, only four patients received antidepressants. There was a significant difference in corticosteroid therapy use between patients with and without depression ($P = 0.046$). However, there was no association between disease activities ($P = 0.661$) or disease duration ($P = 1.00$) and depression. Neither

Table 2: Demographic characteristics of patients with systemic lupus erythematosus ($n = 68$)

Characteristic	<i>n</i> (%)
Median age (range), years	30 (16–59)
Gender	
Male	4 (5.9)
Female	64 (94.1)
Marital status	
Single	33 (48.5)
Married	33 (48.5)
Divorced	2 (2.9)
Education	
Elementary	6 (8.8)
Secondary	33 (48.5)
Bachelor	26 (38.2)
None	3 (4.4)
Income group	
Low	4 (5.9)
Intermediate	41 (60.3)
High	23 (33.8)
Present employment	
No	57 (83.8)
Yes	11 (16.2)

positive aPL ($P = 0.284$) nor APS ($P = 0.738$) was associated with depression [Table 4].

DISCUSSION

Depression is one of the most commonly reported neuropsychiatric symptoms in patients with SLE. However, the prevalence of depression shows a considerable variability (16–60%) in distinct populations.^[8,13-15] The present study indicated a high prevalence (67.6%) of depression in Saudi patients with SLE. We used the validated Arabic BDI to assess the presence of depression. Although Zakeri *et al.* reported a high prevalence (60%) of depression among Iranian patients with SLE,^[8] the prevalence rate was lower than that found in the present study. The higher prevalence of depression in the present study could be because of various factors such as differences in assessment methods, length of follow-up, sample sizes and cultural and social backgrounds. The authors hypothesize that cultural and social differences regarding the acceptance of chronic illness as well as the unique lifestyle practices by women in Saudi Arabia can substantially increase the pressure on patients, particularly females, and thus impact their mental health. For instance, there was no difference in employment status between patients with and without depression in our study, which could be

Table 3: Clinical characteristics and treatment details of patients with systemic lupus erythematosus (n = 68)

Characteristic	n (%)
Suicidal ideation	
No	67 (98.5)
Yes	1 (1.5)
Suicide attempt	
No	68 (100)
Yes	0
Disease exacerbation	
No	46 (67.6)
Yes	22 (32.4)
Comorbid condition	
No	51 (75.0)
Yes	17 (25.0)
SLEDAI score	
No activity (0)	11 (16.2)
Mild activity (1–5)	25 (36.8)
Moderate activity (6–10)	21 (30.9)
High activity (11–20)	8 (11.8)
Very high (≥20)	3 (4.4)
Use of steroid at study enrollment	
No	12 (17.6)
Yes	56 (82.4)
Immunosuppressive therapy	
No	22 (32.4)
Yes	46 (67.6)
Immunosuppressive drugs	
Azathioprine	19 (27.9)
Cyclosporine	1 (1.5)
Cyclosporine/Mycophenolate mofetil	4 (5.9)
Hydroxychloroquine	41 (60.3)
Methotrexate	1 (1.5)
Mycophenolate mofetil	20 (29.4)
Rituximab/Azathioprine	1 (1.5)
No drugs	21 (30.9)
Antidepressant	
No	64 (94.1)
Yes	4 (5.9)
aPL status	
Negative	49 (72.1)
Positive	19 (27.9)
APS	
No	57 (83.8)
Yes	11 (16.2)
BDI score	
No depression (0–9)	22 (32.4)
Mild (10–18)	23 (33.8)
Moderate (19–29)	14 (20.6)
Severe (30–63)	9 (13.2)

APS – Antiphospholipid syndrome; aPL – Antiphospholipid;
SLEDAI – Systemic Lupus Erythematosus Disease Activity Index;
BDI – Beck depression inventory

Table 4: Differences in demographic and clinical characteristics between patients with and without depression

Variables	Patients without depression	Patients with depression	P
Sex			
Male	2 (50)	2 (50)	0.590
Female	20 (31.3)	44 (68.8)	
Marital status			
Single	12 (36.4)	21 (63.6)	0.728
Married	10 (30.3)	23 (69.7)	
Divorced	0	2 (100)	
Education			
Elementary	2 (33.3)	4 (66.7)	0.855
Secondary	9 (27.3)	24 (72.7)	
Bachelor	10 (38.5)	16 (61.5)	
No education	1 (33.1)	2 (66.7)	
Income			
Low	1 (25)	3 (75)	0.403
Intermediate	11 (26.8)	30 (73.2)	
High	10 (43.5)	13 (56.5)	
Employee status			
No	19 (33.3)	38 (66.7)	1.000
Yes	3 (27.3)	8 (72.7)	
Suicidal idea			
No	22 (32.8)	45 (67.2)	1.000
Yes	0	1 (100)	
Disease exacerbation			
No	17 (37.0)	29 (63.0)	0.241
Yes	5 (22.7)	17 (77.3)	
Disease duration (months)			
≤6	1 (33.3)	2 (66.6)	1.00
≥6	21 (32.3)	44 (67.7)	
SLEDAI score			
No activity (0)	4 (36.4)	7 (63.6)	0.661
Mild activity (1–5)	7 (28.0)	18 (72)	
Moderate activity (6–10)	9 (42.9)	12 (57.1)	
High activity (11–20)	2 (25.0)	6 (75.0)	
Very high (≥20)	0	3 (100)	
Steroid use			
No	7 (58.3)	5 (41.7)	0.046
Yes	15 (26.8)	41 (73.2)	
Immunosuppressive therapy			
No	9 (40.9)	13 (59.1)	0.297
Yes	13 (28.3)	33 (71.7)	
Antidepressant			
No	19 (29.7)	45 (70.3)	0.096
Yes	3 (75.0)	1 (25.0)	
Comorbidities			
No	15 (29.4)	36 (70.6)	0.369
Yes	7 (41.2)	10 (58.8)	
aPL			
Negative	14 (28.6)	35 (71.4)	0.284
Positive	8 (42.1)	11 (57.9)	
APS			
No	18 (3.6)	39 (68.4)	0.738
Yes	4 (36.4)	7 (63.6)	

All values are presented as n (%). APS – Antiphospholipid syndrome;
aPL – Antiphospholipid; SLEDAI – Systemic lupus erythematosus disease activity index

explained by cultural background where most of the females were dependent. Many depressive symptoms such as lethargy and increased pain overlapped with SLE symptoms and resulted in delayed or undiagnosed depression.

This study assessed if factors such as patients' characteristics, disease duration and activity, drug therapy and APS contribute to increased prevalence of depression in patients with SLE.^[8] The results showed that there was no association between disease duration, disease activity or immunosuppressive therapies and BDI scores. The findings of the present study are in accord with the findings of other studies using SLEDAI.^[16-18] Using corticosteroids was the only factor that was associated with high BDI scores. However, no association was found between corticosteroid dose and depression ($P = 0.516$), as most of the study population (93%) were on low dose (≤ 15 mg) at the time of enrollment. In previous studies, depression was reported to be associated with corticosteroid therapies.^[19-21] In contrast, in a study that demonstrated major depression in patients with SLE, there was no significant difference in the mean dose of prednisone between SLE patients with and without major depression.^[19] These discrepancies could be explained by variable doses and durations of corticosteroids in different studies. Nevertheless, the association between corticosteroids and depression reinforces the need to minimize the dose and duration of exposure as much as possible to avoid inducing depression. Interestingly, in a study conducted to evaluate the effectiveness of treating lupus nephritis with an oral steroid-free regimen, 90% of patients achieved complete or partial remission at a median time of 37 weeks.^[22] Such encouraging results have huge potential benefits for patients with SLE because they may help avoid the steroid-related side effects, particularly mood and cognitive changes. We did not find any association between the presence of aPL or APS and depression, which was consistent with findings of previous studies.^[21,23]

Another important finding was the low proportion of patients (~6%) receiving antidepressants. van Exel *et al.* also reported a similar finding that only 7% of patients with SLE had received antidepressants.^[16] This finding, in our opinion, reflects inadequate recognition and treatment of depression in SLE. Consequently, we strongly recommend that patients with SLE should be routinely and carefully evaluated for depressive symptoms. When depression is suspected, adequate psychiatric consultation and appropriate treatment are necessary.

There were some limitations in our study. First, we used a self-reported questionnaire that, in a cross-sectional study, could have resulted in over- or understating certain findings. Second, this study had a relatively small sample size, and thus further studies should be conducted with a larger sample size to confirm the findings of this study. Finally, as most participants of the study were female, the findings of this study have limited generalizability.

As this was a multicenter study carried out in different regions of Saudi Arabia, we were able to estimate the prevalence rate of depression among Saudi patients with SLE, assess factors that might be related to depression and detect the important association with corticosteroids. To the best of our knowledge, this is the first-of-its-kind study conducted in Saudi Arabia.

CONCLUSIONS

The study demonstrates high prevalence of depression among Saudi patients with SLE and highlights the need for routine and careful evaluation for depressive symptoms among these patients. Adequate psychiatric consultation and appropriate treatment are necessary in patients with SLE.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Rahman A, Isenberg DA. Systemic lupus erythematosus. *N Engl J Med* 2008;358:929-39.
2. Bertsias GK, Boumpas DT. Pathogenesis, diagnosis and management of neuropsychiatric SLE manifestations. *Nat Rev Rheumatol* 2010;6:358-67.
3. Palagini L, Mosca M, Tani C, Gemignani A, Mauri M, Bombardieri S. Depression and systemic lupus erythematosus: A systematic review. *Lupus* 2013;22:409-16.
4. Bertsias GK, Ioannidis JP, Aringer M, Bollen E, Bombardieri S, Bruce IN, *et al.* EULAR recommendations for the management of systemic lupus erythematosus with neuropsychiatric manifestations: Report of a task force of the EULAR standing committee for clinical affairs. *Ann Rheum Dis* 2010;69:2074-82.
5. Nery FG, Borba EF, Viana VS, Hatch JP, Soares JC, Bonfá E, *et al.* Prevalence of depressive and anxiety disorders in systemic lupus erythematosus and their association with anti-ribosomal P antibodies. *Prog Neuropsychopharmacol Biol Psychiatry* 2008;32:695-700.
6. Johnson RT, Richardson EP. The neurological manifestations of systemic lupus erythematosus. *Medicine (Baltimore)* 1968;47:337-69.

7. Buchbinder R, Hall S, Littlejohn GO, Ryan PF. Neuropsychiatric manifestations of systemic lupus erythematosus. *Aust N Z J Med* 1988;18:679-84.
8. Zakeri Z, Shakiba M, Narouie B, Mladkova N, Ghasemi-Rad M, Khosravi A. Prevalence of depression and depressive symptoms in patients with systemic lupus erythematosus: Iranian experience. *Rheumatol Int* 2012;32:1179-87.
9. Hanly JG, Su L, Urowitz MB, Romero-Diaz J, Gordon C, Bae SC, *et al.* Mood disorders in systemic lupus erythematosus: Results from an international inception cohort study. *Arthritis Rheumatol* 2015;67:1837-47.
10. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: Meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med* 2000;160:2101-7.
11. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, *et al.* The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982;25:1271-7.
12. West J. An Arabic validation of a depression inventory. *Int J Soc Psychiatry* 1985;31:282-9.
13. Purandare KN, Wagle AC, Parker SR. Psychiatric morbidity in patients with systemic lupus erythematosus. *QJM* 1999;92:283-6.
14. Kozora E, Ellison MC, West S. Depression, fatigue, and pain in systemic lupus erythematosus (SLE): Relationship to the American College of Rheumatology SLE neuropsychological battery. *Arthritis Rheum* 2006;55:628-35.
15. Kawakatsu S, Wada T. Rheumatic disease and depression. *Nihon Rinsho JPN J Clin Med* 2001;59:1578-82.
16. van Exel E, Jacobs J, Korswagen LA, Voskuyl AE, Stek M, Dekker J, *et al.* Depression in systemic lupus erythematosus, dependent on or independent of severity of disease. *Lupus* 2013;22:1462-9.
17. Moldovan I, Katsaros E, Carr FN, Cooray D, Torralba K, Shinada S, *et al.* The patient reported outcomes in lupus (PATROL) study: Role of depression in health-related quality of life in a Southern California lupus cohort. *Lupus* 2011;20:1285-92.
18. Kellner ES, Lee PY, Li Y, Switaneck J, Zhuang H, Segal MS, *et al.* Endogenous type-I interferon activity is not associated with depression or fatigue in systemic lupus erythematosus. *J Neuroimmunol* 2010;223:13-9.
19. Nery FG, Borba EF, Hatch JP, Soares JC, Bonfá E, Neto FL., Major depressive disorder and disease activity in systemic lupus erythematosus. *Compr Psychiatry*. 2007; 48:14-9.
20. Shah M, Chaudhari S, McLaughlin TP, Kan HJ, Bechtel B, Dennis GJ, *et al.* Cumulative burden of oral corticosteroid adverse effects and the economic implications of corticosteroid use in patients with systemic lupus erythematosus. *Clin Ther* 2013;35:486-97.
21. Huang X, Magder LS, Petri M. Predictors of incident depression in systemic lupus erythematosus. *J Rheumatol* 2014;41:1823-33.
22. Condon MB, Ashby D, Pepper RJ, Cook HT, Levy JB, Griffith M, *et al.* Prospective observational single-centre cohort study to evaluate the effectiveness of treating lupus nephritis with rituximab and mycophenolate mofetil but no oral steroids. *Ann Rheum Dis* 2013;72:1280-6.
23. Sanna G, Bertolaccini ML, Cuadrado MJ, Laing H, Khamashta MA, Mathieu A, *et al.* Neuropsychiatric manifestations in systemic lupus erythematosus: Prevalence and association with antiphospholipid antibodies. *J Rheumatol* 2003;30:985-92.