Evaluation of depression and general health assessment among systemic lupus erythematosus patients in relation to disease activity and damage

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Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune illness defined by involvement of several systems and variety of clinical symptoms among them the neuropsychiatric manifestations. The purpose of the study was to evaluate the presence of depression and to assess overall health in individuals with SLE, as well as their relation to SLE disease activity and damage. Sixty adult SLE patients were enrolled, along with sixty age and sex-matched controls. For the presence of major depression, all patients were examined using the Beck Depression Inventory (BDI-II) and the General Health Questionnaire (GHQ-12) for mental distress. Antinuclear antibody, anti-ds DNA, complements 3 and 4, and anti-ribosomal P antibody were performed for SLE patients. The SLEDAI-2K and SLEDDI were assessed.

Results: The 60 patients were 52 (86.7%) females and 8 (13.3%) men, with a mean age of 32.5 ± 11.5 years and disease duration of 3.57 ± 3.55 years. Patients with depression accounted for 43 (71.6%) of the total, whereas controls accounted for just 14 (23.3%). Patients with substantial depression had significantly higher SLEDAI-2 K, SLEDDI, and illness duration than those without major depression (p = 0.047, p = 0.043, and p = 0.033, respectively). The patients’ mean GHQ-12 score was 17 ± 5.96, whereas the control group's was 10.0 ± 67.30, with a p value of 0.002. SLEDAI-2 K, SLEDDI, and depression score had a substantial positive association (p = 0.001, p = 0.042), while BDI-II and GHQ-12 had a significant positive correlation (p < 0.001).

Conclusions: Depression and psychological distress were both common in SLE patients. Depression severity was linked to illness duration, activity, and damage.

Keywords: Depression, Systemic lupus erythematosus, SLEDAI-2 K, General health

Background

Systemic lupus erythematosus (SLE) is a chronic autoimmune illness defined by involvement of several systems with variety of clinical manifestations as a result of autoantibody production and immune complex deposition. During their reproductive years, females are nine times more likely than males to be afflicted [1].

In patients with SLE, neuropsychiatric SLE (NPSLE) refers to a diverse range of neurological and psychiatric symptoms caused by involvement of the central, peripheral, and autonomic nervous systems [2, 3]. Seizures, mood disorder, psychosis, headache, neuropathy, and stroke were among the neuropsychiatric symptoms of SLE documented in Egyptian patients [4]. Cognitive impairment was also discovered to be a common symptom in SLE Egyptian patients [5].
Prevalence, initiation time, complexity, resolution rates, and recurrence of neuropsychiatric episodes vary [6]. The majority of the events are linked to a decrease in self-reported health-related quality of life [7]. In a recent research of Egyptian SLE patients, quality of life was shown to be severely impaired, particularly in those who were obese [8].

Mood disorders, particularly depression, are common in SLE patients and are important neuropsychiatric manifestations of the illness, in addition to their high incidence and possible deleterious influence on disease progression [9].

SLE depression is complex, with neurotransmitter dysfunction and immunological activation (lymphocyte abnormalities and cytokine production) being two possible causes [10, 11]. Depression exacerbates pain, tiredness, psychological stress, and reduces treatment adherence in SLE patients, resulting in a considerable worsening in quality of life and job disability [12, 13].

The goal of this study was to evaluate the occurrence of depression and its contributing factors, as well as overall health assessment in patients with SLE, and to determine their relation with disease activity and damage.

Methods
Sixty adult SLE patients who met the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria were included in this research [14]. Patients were recruited from the Rheumatology Unit of Alexandria University Hospital’s Internal Medicine Department. As controls, sixty healthy adults were enlisted who were age and sex matched to the patients. Exclusion criteria included patients with history of depression prior to the onset of SLE, uncooperative patients, antiphospholipid syndrome, other autoimmune rheumatic diseases, and pregnant lupus patients. After receiving clearance from the institutional ethics committee, the study was carried out in accordance with the Declaration of Helsinki’s ethical criteria, and each subject gave their informed consent.

Age, gender, domicile, marital status, educational level, and work status of the participants were all taken into account. All SLE patients had a history taking, a clinical examination, and a disease activity evaluation using the SLE disease activity index (SLEDAI-2k) [15], with scores ranging from “inactive” (scores ≤ 4) to mild-moderate (5–9) to high (≥ 10). The Systemic Lupus Collaborating Clinics/ACR damage index (SLICC/ACR DI) was also used to quantify disease damage [16].

Complete blood count, creatinine, urinary protein to creatinine ratio (PCR), alanine transaminase, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were performed. Serological tests included antinuclear antibodies (ANA), anti-double-stranded DNA (anti-ds DNA), antiribosomal-p antibody, and complement C3 and C4 were among the laboratory tests performed for the patients.

The Beck Depression Inventory Score (BDI-II) was applied to assess the presence of depression in the patients and control group, and we used the Arabic version (Additional file 1), which is one of the most extensively used tools for measuring depression symptoms and severity [17]. It has 13 items, each of which is assessed on a four-point Likert scale ranging from 0 (not likely to happen) to 3 (always or mostly happen). The total number of components in the patient’s score ranges from 0 to 39. There are four levels of depression: no depression (0 to 4), mild cases (5 to 7), moderate instances (8 to 15), and severe cases (≥ 16).

The General Health Questionnaire-12 (GHQ-12) [18] was used to conduct psychometric testing for general health and psychological distress. The GHQ-12 is a 12-item questionnaire with a score range of 1 to 36, with mild cases falling between (1 to 12), moderate cases (13 to 24), and severe cases (25 to 36).

Statistical analysis
IBM-SPSS statistical program version 22 was used to analyze the data. The Mann-Whitney or Student t-test was used to analyze continuous data, while the chi-square test was employed to assess categorical ones. The Spearman coefficient was used to determine the correlation between quantitative variables. Logistic regression analysis was used to determine risk factor for presence of depression among SLE patients. The significance of the acquired results was assessed at a 5% level. The p value of 0.05 was used to determine statistical significance.

Results
The 60 patients had a mean age of 32.5±11.5 years and illness duration of 3.57±3.55 years, with 52 (86.7%) females and 8 (13.3%) men (F to M 6.5:1). Table 1 shows the socio-demographic characteristics of SLE patients and controls. Table 2 shows the patients’ clinical features and immunological profiles. In terms of SLE disease activity, 11 patients had inactive disease, 32 patients had mild-moderate disease activity, and 17 patients had high disease activity. The neuropsychiatric manifestations were observed in 15 patients (25%) and included seizures 3 patients (20%), cranial neuropathy 2 patients (13.4%), psychosis 3 patients (20%), cognitive dysfunction 4 patients (26.6%), headache 3 patients (20%), and peripheral neuropathy 2 patients (13.4%).

The medications that were used by the patients included the following: hydroxychloroquine 52 patients...
(86.6%), glucocorticoids 48 patients (80%), azathioprine 21 (35%), mycophenolate mofetil 9 patients (15%), cyclophosphamide 12 patients (20%), methotrexate 5 patients (8.4%), and cyclosporin 4 patients (6.7%).

According to the BDI-II, 43 (71.6%) of patients experienced depression, with a mean score of $14.94 \pm 7.3$, whereas 14 (23.3%) of the control group's had depression, with mean score of $7.1 \pm 3.62$ (Fig. 1), with a $p$ value of 0.0019.

The SLE patients with depression were classified as following: 17 patients with high disease activity (10 patients in severe depression, 5 patients in moderate depression and 2 patients in mild depression), while 24 patients with mild-moderate activity (2 patients in severe depression, 12 patients in moderate depression and 10 patients in mild depression) and 2 patients were inactive disease had mild depression. Based on the degree of their depression, the patients were separated into three groups: there were 14 individuals with mild depression, 17 with moderate depression, and 12 with severe depression. In addition, there was a substantial distinction between the two groups as regard GHQ-12 with $p$ value = 0.0021 (Fig. 2).

The sociodemographic status of SLE patients with and without depression did not differ substantially, although they did differ considerably in terms of illness duration, SLEDAI-2 K, and SLEDDI ($p$ = 0.033, $p$ = 0.047, and $p$ = 0.043, respectively).

SLEDAI-2 K had a substantial positive connection with BDI-II and GHQ-12 scores ($p < 0.001$), as shown in Fig. 3. SLEDDI was also shown to be associated with depression score ($p = 0.042$) and GHQ-12 severity ($p = 0.026$). Furthermore, there was a significant positive connection between the BDI-II and GHQ-12 ($p < 0.001$).

Anti-ribosomal P antibody testing was positive in 23.3% of SLE patients in this investigation, with a mean titer of 46.48 U/ml. Furthermore, there was a high statistical correlation between anti-ribosomal P antibody and depression score ($p = 0.0472$), as well as SLEDAI-2 K ($p = 0.001$).

Multivariate regression analysis was done to determine the predictors of depression in SLE patients. We found that disease activity, damage, and disease duration were significant predictors for depression (Table 3).

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*(Tables and figures are not included in the plain text representation.)*

**Table 1** Sociodemographic data of SLE patients and the control group

| Parameter          | Group I SLE patients | Group II Control | $p$  |
|--------------------|----------------------|------------------|------|
| Age                |                      |                  |      |
| Range              | 15–55                | 16–65            | 0.236|
| Mean               | 32.56                | 34.63            |      |
| S.D.               | 11.51                | 12.12            |      |
| Sex                |                      |                  |      |
| Male               | 8                    | 13.3             | 0.101|
| Female             | 52                   | 86.7             |      |
| Residence          |                      |                  |      |
| Rural              | 24                   | 40.0             | 0.39 |
| Urban              | 36                   | 60.0             |      |
| Education          |                      |                  |      |
| Not educated       | 8                    | 13.3             | 0.107|
| Read and write     | 22                   | 36.7             |      |
| Preparatory        | 6                    | 10.0             |      |
| Secondary          | 14                   | 23.3             |      |
| University         | 10                   | 16.7             |      |
| Marital status     |                      |                  |      |
| Single             | 16                   | 26.7             | 0.256|
| Married            | 33                   | 55.0             |      |
| Divorced           | 7                    | 11.6             |      |
| Widow              | 4                    | 6.7              |      |
| Occupation         |                      |                  |      |
| Unemployed         | 39                   | 65.0             | 0.09 |
| Employed           | 21                   | 35.0             |      |
| Socioeconomic status |                  |                  |      |
| High               | 2                    | 3.4              | 0.211|
| Moderate           | 8                    | 13.3             |      |
| Low                | 28                   | 46.6             |      |
| Very low           | 22                   | 36.7             |      |

**Table 2** Clinical characteristics, immune profile, and disease activity of systemic lupus erythematosus patients

| Parameter                  | SLE patients (n = 60) |
|----------------------------|-----------------------|
| Clinical                   |                       |
| Mucocutaneous             | 31                    |
| Musculoskeletal            | 28                    |
| Hematological              | 16                    |
| Renal                      | 24                    |
| Neuropsychiatric           | 15                    |
| Cardiovascular             | 9                     |
| Respiratory                | 13                    |
| Immune profile             | Mean ± SD              |
| ANA                        | 179.74 ± 191.36       |
| Anti-ds DNA                | 269.47 ± 229.35       |
| C3                        | 54.57 ± 26.15         |
| C4                         | 12.64 ± 8.91          |
| Anti-ribosomal p antibody  | 46.48 ± 74.76         |
| SLEDAI-2 K                 | Mean ± SD              |
| SLICC/ACR DI               | Mean ± SD              |
|                            | 16.9 ± 9               |
|                            | 3.17 ± 1.3             |
Discussion

SLE has a significant influence on people's quality of life, posing several obstacles, particularly for young people who are frequently impacted. Involvement of the central nervous system (CNS) in SLE is linked to a variety of neurological and psychiatric symptoms and is one of the leading causes of morbidity and disability [19, 20].

The majority of the SLE patients in this study reported significant depressive symptoms. According to the BDI-II score, 43/60 (71.6%) of the patients had depression, while only 14/60 (23.3%) of the control group had depression. This is consistent with Raafat et al. [21], who found that 64% of their study patients had depression, while Stoll et al. [22] found that the prevalence of depression...
was as low as 16%. Our sample had a larger proportion of patients with depression than previous research, which might be related to different methodology, different evaluation tools, patient samples, sample sizes, and different social and economic factors and cultural backgrounds.

GHQ-12 has become one of the most commonly used tools for detecting psychological distress. It carries advantage when compared to other version like GHQ-28, being brief, easily scored. In addition to level of symptoms present (Likert type scoring). It is composed of positive and negative phrased items that cover the multiple dimension of mental health including social dysfunction, anxiety, depression, and loss of confidence [23].

Patients with depression had a higher SLEDAI-2K score than those without, and there was a strong positive connection between SLEDAI-2K score and depression severity. These findings back up the theory that disease activity may be a risk factor for the
Depression is quite common among SLE patients. Disease activity, damage, and disease duration were all found to be predictive of the occurrence and severity of depression. Anti-ribosomal P antibody was found to be positive in considerable number of patients with a significant correlation with depression score. The early identification and treatment of depression may have a significant influence on the patient’s quality of life.

### Conclusions

### Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s43166-022-00113-5.

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### Authors’ contributions

Ahmed Shaaban: software, writing original draft. Manal Tayel: supervision, conceptualization. Eman Hassan: conceptualization, methodology. Medhat Salah: methodology, resources. Mohamed Ibrahim: investigations. Walaa Saide: software, investigations. The author(s) read and approved the final manuscript.

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### Availability of data and materials

Data is available from Ahmed Shaaban (corresponding author).

### Declarations

#### Ethics approval and consent to participate

After receiving clearance from the institutional ethics committee, the study was carried out in accordance with the Declaration of Helsinki’s ethical criteria, and each subject gave written informed consent.

#### Consent for publication

All authors revised the manuscript and approved the publication.

#### Competing interests

The authors declare that they have no competing interests.

### Additional file 1.

**Table 3** Multiple logistic regression analysis of different risk factors affecting depression

| Model       | Unstandardized Coefficients | Standardized Coefficients | Test | p-value |
|-------------|-----------------------------|---------------------------|------|---------|
|             | B              | Std. error | Beta | t      |        |
| (Constant)  | 4.239          | 0.748      |      | 5.666  | 0.000  |
| Age         | −0.003         | 0.012      | −0.058| −0.264 | 0.794  |
| Sex         | −0.083         | 0.337      | −0.047| −0.247 | 0.807  |
| Disease duration | 0.022          | 0.037      | 0.126 | −2.591 | 0.046* |
| SLEDAI score | 0.023          | 0.020      | 0.219 | 3.104  | 0.028* |
| SLEDDI score | 0.401          | 0.173      | 0.406 | 2.580  | 0.0433*|

*p value ≤ 0.05 statistical significance

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**Abbreviations**

ANA: Anti-nuclear antibodies; anti-ds DNA: Anti-double-stranded DNA; BDI-II: Beck Depression Inventory; CNS: Central nervous system; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; GHQ-12: General Health Questionnaire; HRQOL: Health-related quality of life; NPSLE: Neuropsychiatric SLE; PCR: Protein to creatinine ratio; SLE: Systemic lupus erythematosus; SLEDAI-2k: SLE disease activity index; SLICC/ACR DI: Systemic Lupus Collaborating Clinics/ACR damage index; SLICC: Systemic Lupus International Collaborating Clinics; SLEDDI: Systemic lupus erythematosus disease damage index.

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**Consent for publication**

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