

Could ICD10 reflect the effect of Anxiety and Depression on Systemic Lupus Erythematosus Disease Burden?

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease that may affect multiple organ systems, including the central nervous system. Psychiatric symptoms, present in the majority of patients with SLE, may have severe consequences for the patients. The aim of the study was to assess the relation between psychological factors (anxiety and depression) and disease activity parameters in SLE patients.

Patients and Methods: This was a matched hospital-based case control study. The study consecutively enrolled 25 patients with SLE who fulfilled the 2012 systemic lupus international collaborating clinics (SLICC) classification criteria for SLE and 25 healthy individuals, matched for age and sex, who served as a control group. Both case and control groups were subjected to clinical and laboratory evaluation of disease activity and psychological assessment according to The International Classification of Mental and Behavioral Disorders tenth revision (ICD-10).

Results: About 52% of patients had depression and 48% had anxiety symptoms, while only 8% of controls reported mild depression and 8% had anxiety symptoms (p values 0.008 and 0.001 respectively). Data also showed highly significant correlation between disease activity measured by SLE disease activity index (SLEDAI) and both depression and anxiety (p<0.01).

Conclusions: Psychiatric manifestations are common in SLE, and they positively correlated with the disease activity. Using ICD-10 as a standardized tool for assessment of anxiety and depression in SLE patients is valuable for future comparisons with other studies on SLE patients.

Keywords: Systemic lupus erythematosus, disease activity, depression, anxiety, ICD 10.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease that may affect multiple organ systems, including the central nervous system⁽¹⁾. The majority of patients with SLE manifest psychiatric symptoms, primarily major depression⁽²⁾. Genetic and environmental factors might crucially contribute to the psychiatric symptoms of SLE although the pathogenesis of these symptoms is still not well understood. Depression and anxiety may also result from serious episode recurring and painful illness, which is usually associated with insomnia, fatigue, and limited functioning^(3,4).

Depression may be the initial symptom prior to SLE diagnosis, and 11 to 39% of the patients report experiencing it⁽⁵⁾. It is four times higher in SLE patients than in a matched non-SLE population.⁶ In addition to depression, anxiety is quite common in SLE patients, often manifested as a reaction to the illness. *Ainiala et al.*⁽⁶⁾ have reported that anxiety disorders were twice as prevalent among SLE patients as compared to non-SLE subjects. Examining anxiety and depression is therefore crucial in SLE patients; especially that overlooking these symptoms may have major consequences on the patients, such as increased incidence of cardiovascular disease⁽⁷⁾, myocardial infarction⁽⁸⁾, decreased quality of life, disability, loss of employment, suicidal ideas and death⁽⁹⁻¹⁰⁾. Different studies use heterogeneous methods for the assessment of anxiety and depression but they often do not correlate those manifestations with disease activity parameters. So far, the International Classification of Mental and Behavioral Disorders tenth revision (ICD-

10) was not used in evaluating SLE patients for anxiety and depression or in correlating these symptoms to disease activity parameters. This study aimed therefore at evaluating the prevalence and severity of depression and anxiety in patients with SLE, according to the ICD-10 tool. Although the 11th revision of ICD was released by the World Health Organization (WHO) in 2018⁽¹¹⁾, data was collected from patients with SLE prior to this release. ICD-10 which is widely accepted and used by psychiatrists was therefore employed for the evaluation of depression and anxiety in this study.

The aim of the study was to assess the relation between psychological factors (anxiety and depression) and disease activity parameters in SLE patients.

PATIENTS AND METHODS

This was a matched hospital-based case control study. The study consecutively enrolled 25 patients with SLE who fulfilled the 2012 systemic lupus international collaborating clinics (SLICC) classification criteria for SLE⁽¹²⁾ and 25 healthy individuals, matched for age and sex, who served as a control group.

Recruitment was completed over the 6-month study duration from rheumatology outpatient clinics of Minya University. Exclusion criteria constituted of depressive episodes that could be caused by psychoactive substance use or organic mental disorders, psychotic symptoms like hallucinations or delusions, depressive stupor, anxiety sustained by a physical disorder, organic mental disorders and psychoactive substance-related disorders.

Disease activity and outcome measures were assessed in all study participants, as well as clinical and laboratory evaluations (urine analysis, 24-hour urinary protein, C reactive protein [CRP], erythrocyte sedimentation rate [ESR], antinuclear antibody [ANA], anti-double-stranded DNA, C3 and C4 levels). The SLE disease activity index (SLEDAI) includes 16 clinical manifestations and 8 laboratory parameters and covers current symptoms and those present 10 days prior to the visit. SLE activity increases with the SLEDAI scores over a possible range of 0 to 105. Scores ranging from 0 to 10 indicate mild activity of SLE, from 10 to 20 moderate activity, from 20 to 45 severe activity, and scores higher than 45 indicate very severe SLE activity⁽¹³⁾. Patients also received a psychological assessment according to clinical descriptions and diagnostic guidelines of the WHO⁽¹³⁾ and to ICD-10, since ICD-11 was not yet released at the time of data collection and analysis.

Ethical consent:

An approval of the study was obtained from Minya University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 18 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) and Fisher's exact test to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed

as mean and standard deviation (SD). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). Spearman's correlation test was used for non-parametric data. P value ≤ 0.05 was considered significant.

RESULTS

Clinical manifestations in SLE patients

The measurements of clinical and laboratory disease activity showed that SLE patients presented many major clinical manifestations. The most common manifestation was photosensitivity found in 21 (84%) patients, followed by arthralgia, skin rash, and alopecia, all found in 17 (68%) patients. In contrast, lymphadenopathy and neurological manifestations were only found in 1 (4%) and 3 (12%) patients, respectively. All patients were treated with disease-modifying anti-rheumatic drugs (DMARDs) and steroids and 7 (28%) of them were also treated with nonsteroidal anti-inflammatory drugs (NSAIDs).

Descriptive psychological data in SLE group compared to the control group

Psychological data comparing the SLE group to the control group are displayed in Table 1 and show that almost half of the patients suffering from SLE had depressive symptoms, among them five (20%) had mild depressive symptoms, 5 (20%) had severe depressive symptoms and three (12%) had moderate depressive symptoms, while only two (8%) control subjects suffered from mild depressive symptoms ($p < 0.01$). Five (20%) patients of the SLE group had recurrent depression while none of the control subjects suffered from it ($p = 0.01$). Seven (28%) SLE patients had somatic symptoms compared to one (4%) subject from the control group but the difference was not statistically significant ($p = 0.02$). Finally, 12 (48%) SLE patients had anxiety, while 2 (8%) subjects from the control group suffered from this condition ($p < 0.01$).

Table (1): Comparison of psychological data in SLE and control groups.

| Variable | SLE patients (n=25) | Control subjects (n=25) | Chi-Square | P value |
|---|---------------------|-------------------------|------------|---------|
| Depressive symptoms | | | | |
| Mild | 5 (20%) | 2 (8%) | 12.74 | 0.005* |
| Moderate | 3 (12%) | 0 (0%) | | |
| Severe | 5 (20%) | 0 (0%) | | |
| Recurrent depression | 5 (20%) | 0 (0%) | 9.92 | 0.01* |
| Somatic symptoms | 7 (28%) | 1 (4%) | 5.36 | 0.02* |
| Anxiety | 12 (48%) | 2 (8%) | 9.92 | 0.001* |
| Chi-Square test/ Fisher's exact test was used to compare categorical data; SLE: systemic lupus erythematosus; * $P \leq 0.05$ indicates significance. | | | | |

Correlation between SLEDAI and psychological data in SLE patients

SLEDAI scores were calculated for patients suffering from SLE. Most of patients with severe

SLEDAI (80%) had severe depression while all patients with a moderate SLEDAI score and more than 50% of patients with a mild SLEDAI score had no depressive symptoms. The correlation of SLEDAI scores with the presence of depressive symptoms was statistically significant ($p=0.009$). A statistical significant correlation was also observed between SLEDAI scores and recurrent depression ($p=0.04$) and anxiety ($p=0.001$) while no significant correlation was shown between SLEDAI scores and somatic symptoms. Correlations between SLEDAI scores and psychological data are further detailed in Table 2.

Table (2): Correlation between SLEDAI and psychological data in SLE patients

| Variable | SLEDAI scores | | | r | P value |
|----------------------|---------------|----------------|--------------|--------|---------|
| | Mild (n=18) | Moderate (n=2) | Severe (n=5) | | |
| Depressive symptoms | | | | 0.514 | 0.009* |
| Mild | 5 (27.8%) | 0 (0%) | 0 (0%) | | |
| Moderate | 2 (11.1%) | 0 (0%) | 1 (20%) | | |
| Severe | 1 (5.6%) | 0 (0%) | 4 (80%) | | |
| Recurrent depression | 2 (11.1%) | 0 (0%) | 3 (60%) | -0.405 | 0.04* |
| Somatic symptoms | 4 (22.2%) | 0 (0%) | 3 (60%) | -0.251 | 0.22 |
| Anxiety | 5 (27.8%) | 2 (100%) | 5 (100%) | 0.642 | 0.001* |

Spearman's correlation test was used; SLEDAI: systemic lupus erythematosus disease index; * $P \leq 0.05$ indicates significance.

DISCUSSION

Our study included 24 female (96%) and one male (4%) patients. Among them, 13 (52%) had depression, 16 (64%) had somatic manifestations and 13 (52%) had anxiety. A high significant correlation was observed between occurrence of depressive symptoms, recurrent depressive episodes and anxiety symptoms and disease activity of SLE patients assessed by SLEDAI.

These were in agreement with a previous study by **Bachen et al.** (15) that was conducted on 326 SLE patients and that revealed a significant correlation between disease activity and chronic major depression ($p=0.001$) and presence of a mood or anxiety disorder ($p=0.001$). Another study by **Shen et al.** (16) followed 170 SLE patients and demonstrated that the severity of anxiety and depression was significantly positively correlated to SLE disease activity as assessed by the SLEDAI index score. However, there was a disagreement with previous findings of **Kheirandish et al.** (17) who carried out a study on 166 SLE patients using SLEDAI and Beck and Cattell inventories for evaluation of depression and anxiety and found no significant association between SLEDAI and depression or anxiety; this disagreement may be due to the use of different scales for depression and anxiety. Another discrepancy with these data was observed in a

study **Maneeton et al.** (18) in which 62 SLE patients (61 females and 1 male) participated. Rates of depression and anxiety in SLE patients were 45.2% and 37.1%, respectively, with no significant relation between SLEDAI and depression or anxiety. There was also a disagreement with **Tay et al.** (19) who studied 110 SLE patients and found that anxiety and depression severity is independent of SLE activity, according to a questionnaire for depression and anxiety other than the ICD-10 international classification of Mental and Behavioral Disorders questionnaire used in the present study.

The study revealed a significantly higher frequency of psychological disorders (depression, anxiety and somatic manifestation) in SLE patients (52%) compared to the control group (20%), which agreed with **Tay et al.** (19) who followed 110 SLE patients and demonstrated that anxiety was significantly higher in SLE patients (40.9%) compared to non-SLE subjects (21.8%) and that depressive symptoms also occurred significantly more frequently in SLE patients (15.5%) compared to non-SLE subjects (6.4%). The importance of understanding the prevalence of depression and anxiety in SLE patients stems from the impact of these psychological disorders on the patients' quality of life. Depressive and anxiety symptoms are associated with poor health-related quality of life and higher likelihood to experience work disability, including lower productivity or ending work (20). The negative impact of depression and anxiety extends to patient sleep, as they significantly contribute to poor sleep quality (21) and fatigue (22) in SLE patients. This highlights the need to consider SLE as a multidisciplinary disease and support informed patient decision to involve several specialists in a collaborative clinical management of this condition.

Limitations: The major limitation of this study is the small sample size of both control and patient study groups; in fact, this study is considered as an exploratory investigation and no sample size calculation was performed. Further investigation is needed with a larger study population and a more consequent follow-up over time, to allow better generalization. This study also used the ICD-10 evaluation tool for depression and anxiety. ICD-11 was more recently released, in 2018, but could not be used for a more up-to-date evaluation as patient data was collected prior to its release date by the WHO.

CONCLUSIONS

Psychiatric manifestations are common in SLE patients and that there is a positive correlation between them and disease activity. In addition, ICD-10 can be used as a standardized tool to evaluate anxiety and depression in SLE patients and in follow-up studies,

which will facilitate comparison to other published works.

RECOMMENDATIONS

The routine evaluation in SLE patients of psychiatric examination, especially depression and anxiety, is crucial due to the strong relation between these manifestations and the activity of the disease. SLE patients see their morbidity increase and their disease outcome worsened by psychological disorders. Hence, the use of tools such as ICD-10 offers deeper insight on the true prevalence of these disorders among SLE patients, providing more accurate and early diagnosis.

This would lead to better clinical care for patients with SLE prior to the development of weakening changes and subsequent physical dysfunctions and impairment of their quality of life. With the release of ICD-11, we strongly recommend the evaluation of the psychological burden that accompanies SLE according to the WHO current guidelines. Recent data suggest that ICD-10 in the evaluation of posttraumatic stress disorder might identify cases less severe compared to ICD-11.²³

Another study explains that posttraumatic stress disorder prevalence is significantly increased under ICD-11 compared to ICD-10.²⁴ When it comes to mental disorders in general, no difference was shown in the accuracy of diagnosis between ICD-10 and ICD-11 but introducing of new diagnosis in ICD-11 has improved the diagnostic classification of some clinical manifestations.²⁵ ICD-11 was therefore considered by mental health professionals as slightly more useful than ICD-10 in the classification of personality disorders²⁶ and further research remains to be carried to better understand the occurrence of anxiety and depression in SLE patients and to identify any discrepancies between ICD-10 and the new classification of ICD-11.

List of abbreviations:

ANA: AntiNuclear Antibody. CRP: C-reactive protein. ESR: Erythrocyte Sedimentation Rate. ICD-10: International Classification of Mental and Behavioral Disorders tenth revision. SLE: Systemic lupus erythematosus. SLEDAI: SLE disease activity index. SLICC : Systemic Lupus International Collaborating Clinics. WHO: World Health Organization.

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