## RESEARCH

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# Impact of depression on quality of life in systemic lupus erythematosus patients



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#### Abstract

**Background:** Depression is common in systemic lupus erythematosus (SLE) and is an unmeasured risk factor, yet its symptoms can be neglected in standard disease evaluations. The purpose of this study was to assess the frequency and the impact of depression on quality of life in SLE patients. We recruited 32 patients with SLE and 15 healthy control volunteers in the study. The following investigations were undertaken in each patient: clinical and rheumatologic assessment, SLE Disease Activity Index-2k (SLEDAI-2k), Beck Depression Inventory (BDI), Short-Form Health Survey (SF-36) questionnaire, and routine laboratory tests.

**Results:** There was a high percentage of depression (46.9%) in the SLE patients. Regarding quality of life (SF-36), there were significant affection of the physical and mental composite summary domains (PCS and MCS) scores in lupus patients compared with controls (P < 0.000 for both) with the same significant in depressed compared with non-depressed patients. SF-36 subscales (physical function, limit emotional, emotional wellbeing, and social function) were significantly affected in depressed lupus patients compared with non-depressed patients. There was a significant negative correlation between the score of MCS domain of SF-36 with BDI (P < 0.000) while positive correlation between SLEDAI score with depression score. In contrast, there were no significant correlations between MCS or PCS with age, duration of illness, or SLEDAI-2K.

**Conclusions:** Depression is common in SLE patients and had a negative impact on quality of life particularly on MCS domain and positive correlation with disease severity score.

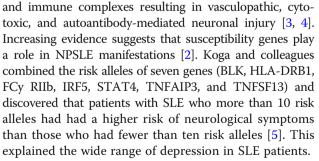
**Trial registration:** This study was registered on clinical trial with registration number: NCT03165682 https:// clinicaltrials.gov/ct2/show/NCT03165682 on 24 May 2017.

Keywords: Systemic lupus erythematosus, Pain, Depression, Disease activity, Physical health

#### Background

Systemic lupus erythematosus (SLE) is a progressive autoimmune disease characterized by a wide range of clinical manifestations and an erratic disease path that includes remissions and exacerbations [1]. Neuropsychiatric systemic lupus erythematosus (NPSLE) is one of the most severe forms of SLE, characterized by psychiatric, central, and peripheral neurological signs and symptoms [2]. The pathogenesis of NPSLE is multifactorial and involves various inflammatory cytokines, autoantibodies,

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The most common microscopic brain finding in SLE seems to be microvasculopathy although not specific, which may be due to complement activation and antiphospholipid antibodies [6]. Using structural MRI, 40–80%

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of abnormalities in NPSLE are multiple discrete lesions concentrated in periventricular and subcortical white matter [7]. Metabolic neuroimaging (positron emission tomography/PET, MR spectroscopy) and perfusion imaging (single photon emission computer tomography/SPECT) can detect abnormalities in patients who present exclusively with psychiatric manifestations. The fluorodeoxyglucose-PET (FDG-PET) imaging can demonstrate white matter hypometabolism of the parieto-occipital in up to 80% of patients [8–10]. The functional near infrared spectroscopy (fNIRS) neuroimaging could also be used to elucidate the pathophysiology of psychiatric disorders and identify neurophysiological differences between co-occurring psychiatric disorders [11, 12].

Patients with major depressive disorders had smaller changes in oxyhemoglobin in the frontal and temporal cortices than normal. Hemodynamic response measured by fNIRS during an English letter fluency task is a promising biomarker for major depressive disorders [11, 12].

Over the past few decades, deaths in people with systemic lupus erythematosus (SLE) have declined [13], allowing care to be refocus on improving health-related quality of life (HRQoL), including effects on an individual's physical, mental, and social function [14]. Like other chronic conditions, SLE patients have a lower HRQoL [15, 16].

Factors that have a negative effect on HRQoL, such as pain, and depression, should be given special consideration, according to the Treat to Target (T2T) guidelines for SLE [17]. Major depression is common in SLE, yet its symptoms are often neglected in standard disease evaluations [18, 19]. A previous study reported a link between major depression in SLE and lower HRQoL [20]. However, details of the relationship, in particular the effects of depression on domains of the HRQoL are not well understood [21]. The present study aimed to determine the impact of major depression on the quality of life of SLE-relevant health domains and to evaluate other possible risk factors that can affect the quality of life.

#### Methods

This case-control study was conducted at the Assiut University Hospital in the period between May 2019 and August 2020. Patients were recruited from the outpatient clinics and inpatients of the Physical Medicine, Rheumatology and Rehabilitation Department, in collaboration with Neuropsychiatry Department, Assiut University Hospital. All the recruited SLE patients had fulfilled the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE [22]. The sample size was estimated using the EPI info statistical package Version 7. The used parameters for determining sample size were a proportion of 0.5, a confidence level of 95% and a margin of error of 5%. In this study, we used a systematic random sample as the first participant who fulfills the study criteria was randomly selected. Then, every second participant was recruited in the study.

A total of 47 participants were recruited; 32 SLE patients met the principal eligibility criteria required for SLE [22], and 15 healthy volunteers matched for age, sex, total years of education, and social backgrounds, were taken as a control group.

The inclusion criteria were (a) age 18 years or older; (b) a consistent drug therapy for the prior three months in SLE patients; (c) no comorbid severe medical conditions such as diabetes, congestive heart failure, or fibromyalgia.

We excluded participants if they had (a) a diagnosis of any other systemic autoimmune disorders; (b) a history of depression before the diagnosis of SLE; (c) pregnancy.

All eligible participants for this study had the following: sociodemographic data included age, sex, employment status, and educational level. For patients with SLE, disease variables such as disease duration (years) and other disease characteristics were also recorded. All study participants underwent a complete medical history and thorough physical examination including neurological system examinations and psychiatric interviews. For patients with SLE, assessment of disease activity was evaluated using the Systemic Lupus Erythematosus Disease Activity Index-2k (SLEDAI-2k), which covers clinical (16 items) and laboratory (8 items) variables [23]. Routine laboratory tests were performed, including complete blood count (CBC), blood sugar, and 24-h urine protein.

#### The Arabic version of Beck Depression Inventory (BDI) [24]

This instrument is a self-reported questionnaire of depressive symptoms over the last 2 weeks, consisting of 21 questions concerning the different domains of depression with a total score ranging from 0 to 63 [25]. All responders scoring higher than 13 points on the BDI were subjected to detailed interviews with research workers trained in mental health.

#### The Arabic version of the Short-Form Health Survey (SF-36) questionnaire [26, 27]

It consists of 36 items measuring 8 subscales: physical function, social function, and role limitations due to physical health problems, role limitations due to emotional problems, mental health, vitality, bodily pain, and general health perceptions. The subscale and summary scores on the SF-36 range from 0 to 100, with higher scores indicating better HRQoL [28].

#### Statistical analysis

Software (SPSS, Version 20.0 for Windows, SPSS Inc., Chicago, IL) was used for analysis of the data. To compare demographic and clinical data among groups, the Mann-Whitney test was used. The median  $\pm$  standard deviation was used to express continuous variables, while number and percentage were used to express categorical variables. To compare the means of more than two groups, the Kruskal-Wallis H test was used. When the P value was less than 0.05, it was considered significant. A non-parametric Spearman's correlation coefficient test was used to investigate correlations between various clinical scales and quality of life parameters because of the abnormal data distribution detected by Shapiro test.

#### Results

#### Sociodemographic and clinical characteristics

Table 1 showed that absence of significant differences in age or education level between the patients and controls. However, there were more non-workers in the SLE group than in the controls. The SLE group with depression had a higher percentage of most clinical signs compared to the non-depressed group but was significant only for arthritis (P = 0.046) (Table 2). There were no significant differences in any of the laboratory investigations between depressed and non-depressed SLE patients.

Regarding HRQoL (SF-36), there were significant affection of the PCS and MCS scores (lower mean score of the both) in lupus patients compared with controls (P = 0.000 for both) with the same significant in depressed patients compared with non-depressed patients.

Concerning the subscales of SF-36 (physical function, limit emotional, emotional wellbeing, and social function), all were significantly affected in depressed lupus patients compared with non-depressed patients. Details illustrated in Table 3.

In Table 4, there was a significant negative correlation between the score of MCS domain of SF-36 with BDI (P < 0.000) while positive correlation between SLE-DAI score with depression score. In contrast, there were no significant correlations between MCS or PCS with age, duration of illness, or SLEDAI-2K (Table 5).

#### Discussion

The important findings in this study are the high percentage of depression in SLE and its negative impact on HRQoL. This contrasts with the absence of significant impacts of the age, duration of illness, and the disease activity as measured by the SELDI scale on HRQoL.

In the current study, most (89.4%) of the patients were female, as in the Mork study which had 92% women [29]. This is consistent with recent systematic reviews which reported that females had a higher frequency of SLE than males, with a sex ratio ranging from 2:1 [30] to 15:1 [31]. The majority of the participants were not in work and had only primary education. Previous studies found that unemployment and lower education levels are associated with depression [32–35].

Our patients were classified into depressed (15 cases 46.9%) and non-depressed groups (17 cases 53.1%) according to their BDI scores. In previous studies, the incidence of depression has varied widely from 8.7 to 78.6%. This wide range may be a consequence of the lack of clarity in the diagnosis of depression and use of different measurement scales or may be related to medical treatment. In a recent systematic review and meta-analysis of 69 studies with a total population of 23,386, the overall prevalence of depression among SLE patients was 35% [36].

In the present study, SLE patients with depression had significantly (0.04) higher % of arthritis compared with non-depressive patients, while no significant differences between groups in other clinical and laboratory data. Dimattew and colleagues also reported that depression could negatively affect treatment outcomes through non-adherence to recommended treatments and clinic appointments [37]. However, when patients are treated

**Table 1** Demographic data of studied groups (SLP group and control group)

	Cases subjects (N = 32)	Control subjects ( <i>N</i> = 15)	P value
Age (mean ± SD)	34.8 ± 10.06	34.6 ± 7.7	0.94
Sex ratio (F/M)	29/3	13/2	0.64
Occupation:			
Non-worker	28(87.5%)	8 (53%)	0.023
Worker	4(12.5%)	7 (47%)	
Education:			
Illiterate	7(21.9%)	3 (20%)	0.74
Primary education	18(56.3%)	10 (66.7%)	
Secondary education	7(21.9%)	2 (13.3%)	

Variables	Total (N = 32)	Depressive group (N = 15)	Non-depressive group (N = 17)	P value
Duration of illness in years (mean ± SD)	6.34 ± 4.5	6.46 ± 5.54	6.23 ± 3.52	0.888
Clinical symptoms N (%)				
Myalgia number N (%)	26 (81%)	13 (87.7%)	13 (76.5%)	0.392
Lupus headache N (%)	25 (78%)	13 (86.7%)	12 (70.6%)	0.254
Arthritis N (%)	22 (69%)	13 (86.7%)	9 (52.9%)	0.046
Alopecia N (%)	22 (69%)	10 (66.7%)	12 (70.6%)	0.555
Oral/nasal ulcers N (%)	22 (69%)	12 (80%)	11 (64.7%)	0.287
Malar rash N (%)	20 (63%)	10 (66.7%)	10 (58.8%)	0.464
Fever N (%)	24 (51%)	13 (86.7%)	11 (64.7%)	0.152
Vasculitis lesion N (%)	4 (13%)	2 (13.3%)	2 (11.8%)	0.650
Retinal disease N (%)	3 (9%)	2 (13.3%)	1 (5.9%)	0.452
Cerebrovascular stroke N (%)	3 (9%)	1 (6.7%)	2 (11.8%)	0.548
Laboratory data (mean $\pm$ SD)				
Protein 24 h in urine (mean $\pm$ SD)	264.84 ± 227.7	231.7 ± 236.7	294.1 ± 222.	0.448
Blood platelets (mean $\pm$ SD)	259.9 ± 64.95	262.3 ± 70.4	257.9 ± 61.9	0.854
Blood WBCs (mean ± SD)	5.78 ± 2	5.9 ± 1.7	5.7 ± 2.4	0.830
Blood sugar (normal range 70–100 mg/dl (mean $\pm$ SD)	88.31 ± 14.22	92 ± 15.5	85.1 ± 12.6	0.172
SLEDAI-2K (mean ± SD)	19.34 ± 7.46	21.6 ± 5.36	17.32 ± 8.58	0.109

Table 2 Duration of illness, clinical symptoms, and laboratory data in relation to depression

SLEDAI-2K the Systemic Lupus Erythematosus Disease Activity Index-2k, WBCs white blood cells

promptly, mood disorders could be resolved in around 50% of patients with SLE [38]. Therefore, recognition of depression and providing adequate treatment for it are essential aspects of optimal management of SLE.

Make and colleagues 2011 reported that anxiety in SLE patients could be predicted by the presence of depression, high dose of cumulative glucocorticoid,

and other regular medications. The severity of depression predicted both the severity and presence of anxiety. Hence, lupus patients who demonstrated anxiety should concomitantly and properly be evaluated for depression [39]. Unfortunately, we did not assess the anxiety in the current study and added it as one of limitation of the study.

	Total (N = 32) (Mean ± SD)	Depressive group (N = 15) (Mean ± SD)	Non-depressive group (N = 17) (Mean ± SD)	Control subjects (N = 15) (Mean ± SD)	P value (depressed vs non-depressed)	<i>P</i> value (between control and total patients' group)
SF-36 scale						
SF-36 physical function	39.3 ± 24.6	20.0 ± 15.1	33.0 ± 17.5	64.3 ± 15.0	0.034	< 0.0001
SF-36 limit physical	19.8 ± 29.2	$1.7 \pm 6.5$	5.0 ± 14.0	51.1 ± 29.0	0.24	< 0.0001
SF-36 limit emotional	47.4 ± 33.7	17.8 ± 24.8	66.7 ± 28.2	57.8 ± 26.6	< 0.0001	< 0.0001
SF-36 energy/fatigue	36.6 ± 12.6	25.3 ± 14.8	37.3 ± 10.8	44.3 ± 7.5	0.09	0.002
SF36 emotional well being	50.3 ± 13.2	38.5 ± 13.9	53.7 ± 13.7	54.6 ± 9.9	0.001	0.001
SF-36 social function	56.3 ± 16.6	47.5 ± 12.7	56.3 ± 17.2	60.2 ± 18.9	0.038	0.88
SF-36 pain	44.9 ± 14.5	38.5 ± 10.8	41.2 ± 11.0	55.2 ± 16.0	0.506	0.002
SF-36 general health	38.8 ± 16.8	28.0 ± 15.3	33.0 ± 9.2	55.0 ± 11.8	0.25	< 0.0001
Physical composite scale (PCS)	35.2 ± 18.0	22.2 ± 9.2	29.5 ± 12.0	53.8 ± 14.4	0.071	< 0.0001
Mental composite scale (MCS)	12.9 ± 4.3	9.1 ± 3.6	14.4 ± 3.1	15.2 ± 3.8	< 0.0001	< 0.0001

**Table 3** The impact of depression on quality of life (SF-36 score)

SF-36 The Short-Form Health Survey

PCS physical composite scale, MCS mental composite scale

**Table 4** Correlation between Beck's Depression Inventory total score and age, duration of illness, SLEDAI-2K, physical composite scale (PCS), and mental composite scale (MCS) in SLP patients

Variables		Beck's depression inventory total score
Age (years)	r	0.046
	P value	0.801
Duration of illness (years)	r	- 0.154
	P value	0.401
SLEDAI-2K	r	0.372
	P value	0.036
Physical composite scale (PCS)	r	- 0.211
	P value	0.262
Mental composite scale (MCS).	r	- 0.688
	P value	< 0.0001

*SLEDAI-2K* The Systemic Lupus Erythematosus Disease Activity Index-2k *PCS* physical composite scale, *MCS* mental composite scale

Skapinakis and colleagues observed that depression could act as independent risk factors in general health care [40]. The SLEDAI-2K scale that measures SLE's activity showed no significant differences between depressed versus non-depressed groups and had no significant correlation with HRQoL (SF-36). This suggests that other issues could contribute to the SLEDAI-2K scores, such as fatigue, difficulty to arrange events/meetings due to the disease's unpredictable course, and a lack of disease awareness in the workplace [41].

The present study showed that SLE patients with depression had worse (lower) SF-36 score than patients without, particularly in physical function, limited emotions, energy/fatigue, and emotional well-being, all of which have an impact on QoL. This was confirmed by the significant inverse correlation between BDI and SF-36. A similar finding was noted by Bertsias and colleagues who recorded that depression was associated with a low HRQoL [42]. The patient's internal understanding of coping with the condition impacts QoL. It suggests a strategy to deal with the disease: with

**Table 5** Correlation between age, duration of illness, SLEDAI-2K with physical composite scale (PCS), and mental composite scale (MCS) in SLP patients

Variable		Physical composite scale (PCS)	Mental composite scale (MCS)
Age (years)	r	- 0.206	0.137
	P value	0.275	0.478
Duration of illness (years)	r	- 0.199	0.083
	P value	0.293	0.670
SLEDAI-2K	r	- 0.232	- 0.348
	P value	0.217	0.065

*SLEDAI-2K* the Systemic Lupus Erythematosus Disease Activity Index-2k, *PCS* physical composite scale, *MCS* mental composite scale

everyday tasks and an expression of hope for a better life [43]. As a result, in daily clinical practice, SLE patients' HRQoL is linked to depression and fatigue to varying degrees.

One of the important limitations of the present study is the small sample size, since large sample sizes are recommended in studies that examine the impact of anxiety and medical treatment on quality of life. This study mainly used self-reported questionnaire (Beck Depression Inventory) to measure psychiatric symptoms and did not make clinical diagnosis. The gold standard for establishing psychiatric diagnosis involved structured clinical interview and functional neuroimaging [11, 12]. Screening for other comorbid psychiatric disorders in SLE patients is also recommended.

#### Conclusion

The present study demonstrated that depression is common in SLE patients and had a negative impact on HRQoL particularly mental function and increase with disease severity.

#### Abbreviations

SLE: Systemic lupus erythematosus; SLEDAI-2k: Systemic Lupus Erythematosus Disease Activity Index-2k; BDI: Beck Depression Inventory; MFIS: Modified Fatigue Impact Scale; SF-36: Short-Form Health Survey; HRQoL: Health-related quality of life; QoL: Quality of life; NPSLE: Neuropsychiatric systemic lupus erythematosus; fNIRS: The Functional near infrared spectroscopy; SLICC: Systemic Lupus International Collaborating Clinics; PCS: Physical composite scale; MCS: Mental composite scale

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None

#### Authors' contributions

EK and GA recruited participants, analysis, and interpreted data, and were the contributors in writing the manuscript. SR and RG revised data interpretation, read, and approved the final manuscript. MJ helped in data entry, analyze, and generate result sheets. All authors have read and approved the manuscript.

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#### Availability of data and materials

All data generated or analysed during this study are available from corresponded on request.

#### Declarations

#### Ethics approval and consent to participate

This study had ethical approval from Institutional Review Board (IRB) of Faculty of Medicine, Assiut University with Approval Number (IRB17100158). This study was registered on clinical trial with registration Number (NCT03165682) https://clinicaltrials.gov/ct2/show/NCT03165682 on 24 May 2017. Written informed consent was obtained from patients to participate in the study. All procedures performed in this study were in accordance with the ethical standard of the institution and/or national research committee and with the 1964 Helsinki Declaration and its later amendments.

#### **Consent for publication**

Not applicable

#### **Competing interests**

The authors declare that they have no competing interests.

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