Anxiety and depression predict quality of life in Turkish patients with systemic lupus erythematosus

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Abstract

Objective

The aim of our study was to evaluate quality of life (QoL) in patients with systemic lupus erythematosus (SLE) and assess the impact of disease activity and psychological distress on health-related quality of life (HRQoL) in Turkey.

Methods

The Medical Outcomes Study Short Form (SF) -36 was used in a cohort of 113 consecutive patients with SLE and 123 age- and gender-matched healthy subjects to measure HRQoL. Patients' disease activity was assessed with SLE disease activity index (SLEDAI) and psychological distress was evaluated by the Hospital Anxiety and Depression Scale (HADS) for all participants. Patients' demographic and clinical data were recorded at the time of HRQoL and HADS testing. Multiple logistic regression analysis was performed to explore the relationships between demographics, disease duration, disease activity as well as psychological (anxiety and depression) variables and the HRQoL.

Results

SLE patients have lower quality of life than healthy controls. No relationship between HRQoL and SLE activity or disease duration were observed. Patients with anxiety and/or depression reported worse SF-36 scores than those without psychological distress. The results of multivariate analysis suggested that HADS-A, HADS-D scores and working status were associated with the impairment of HRQoL.

Conclusion

HRQoL is impaired in patients with SLE and is associated with mood disorders. Physicians should pay close attention to detect anxiety and depression and manage them in order to improve the quality of life in patients with SLE.

Key words

systemic lupus erythematosus, quality of life, anxiety, depression

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Introduction

Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease characterised by a varying, heterogenous disease activity over time and potentially involve most organ systems during the disease course. The remission and exacerbation phases may follow each other and sometimes the effects of the disease may be irreversible. For these reasons, SLE may affect quality of life in patients unfavourably, leading to poorer health-related quality of life (HRQoL) (1).

There are studies indicating that the quality of life in patients with lupus is affected by psychosocial and behavioural factors other than disease activity and damage (3, 4). Furthermore, it has been shown that depression, anxiety and psychosis are the most commonly described disorders during the disease course (5, 6). Psychological distress and its impact on HRQoL in patients with SLE have been investigated in many studies and it was found as the best predictor of life quality in lupus patients (7-9). Therefore physicians should assess not only objective signs and symptoms of the disease, but also psychological, mental and social burdens of SLE on patients' daily life (2).

During the assessment of a patient with lupus, incorporating patient-reported outcomes into research has been recommended by the Outcome Measures in Rheumatology Clinical Trials (OMERACT) (10) to cover both the disease activity and its impact on patient's health status. The use of HRQoL instruments as secondary outcome measures for SLE clinical trials is also recommended in the European League Against Rheumatism (EULAR) guidelines (11).

The 36-item Short Form Health Survey (SF-36) is a generic tool and the most frequently used instrument in rheumatology (12, 13).

The aim of our study was to evaluate QoL in SLE patients compared with healthy controls and assess impacts of disease activity and mental health on HRQoL in Turkish SLE patients.

Material and methods

One hundred and thirteen consecutive patients with SLE followed at the Marmara University Medical Faculty Rheumatology outpatient clinics in Istanbul, Turkey and 123 age- and gender-matched healthy subjects were enrolled as controls in this cross-sectional study. The exclusion criteria for patients and controls were a history of psychiatric disease and being under 18 years of age. Patients with neuropsychiatric involvement were also excluded. Healthy controls were randomly selected out of participants accompanying lupus patients during their visits, without any symptoms and were not family members or close relatives of patients. The disease was classified according to the American College of Rheumatology (ACR) classification criteria for lupus (14) and the disease activity was measured by the SLE disease activity index (SLEDAI) (15). SLEDAI score ranges between 0–105: 0, means no activity; 1–5, mild activity; 6–10, moderate activity; 11–19, high activity; and ≥20 means very high activity. Physician's global assessment (PGA) was also used to evaluate disease activity with scores ranging from 0–3. The SLEDAI index and PGA were scored by the same physician who was blinded to the results of the questionnaires when scoring. PGA score of "0" means inactive, "1" mild, "2" moderate and "3" means high disease activity. All of the participants gave written informed consent and the study was approved by Marmara University local ethics committee.

The patients and the controls were invited to complete the questionnaires of HRQoL and Hospital Anxiety and Depression Scale (HADS) on the same day with their visit. To rule out the bias that could result from the different education levels of participants, the questionnaires were administered by a study nurse who was blinded to the demographic and clinical features of the patients. QoL was evaluated with SF-36. It is composed of eight domains which of four are physical (physical functioning, physical role limitation, bodily pain and general health) and the other four are mental (social functioning, emotional role limitation, mental health and vitality) components (16). The scales, physical and mental summary scores (PCS, MCS) range from 0

(means the worst QoL) to 100 (means the best QoL). Impaired SF-36 subscale scores on each SF-36 domain were determined as values lower than the mean values observed for the entire study population.

Anxiety and depression were assessed using the HADS. Scores of 8–10 indicate possible, scores of 11–14 indicate probable and scores of 15–21 indicate extreme cases of depression and anxiety (17, 18). A score over 8 points is accepted as the presence of anxiety and depression.

Demographic (age, sex, marital, educational and working status) and clinical data (a complete history, duration of SLE, disease activity, immunological evaluations, physical examination and laboratory tests) were recorded for each patient at the study inclusion.

Statistics

Descriptive statistical analysis was presented as mean±SD in normal distributions and median and interquartile ranges in non-normally distributed data. Comparisons between groups were made using Student's *t*-test for continuous variables and chi-square test for categorical variables. The relationship between continuous variables were examined with Pearson's correlation coefficient. Univariate linear regression analyses were used to specify the relationships between age, disease duration, education time, SLEDAI and SF-36 subscales. Multivariate logistic regression models with stepwise backward elimination were used to determine the ability of psychological and demographical parameters to independently predict SF-36 scores. Statistical analyses were performed using the Software Statistical Package Sciences (SPSS) for Windows version 16.0. All *p*-values <0.05 were considered statistically significant.

Results

Demographic and clinical features

The mean (±SD) age was 40.6±11.9 and 40.7±11.5 years in SLE patients and healthy controls, respectively (p=0.976). One hundred and eight patients and one hundred and eight (108) controls were female (p=0.056). The median disease duration was 6 (0.25–35) years. 82.2% of patients were married. In control group, 90 participants were married (p=0.111). 77% and 82.9% of patients and healthy controls were not employed, respectively (p=0.069). The education levels of 71 (62.9%) patients and 84 (68.2%) healthy controls were elementary school or less; 23 (20.4%) patients and 16 (13.0%) controls were high school and the remaining members of two groups were college or more (p=0.155). Eighty-four (69%) patients had active disease; of these patients 40 (35.4%), 28 (24.8%), 8 (7.1%) and 2 (1.8%) had mild, moderate, high and very high disease activity according to SLEDAI, respectively. 66 (58.4%) patients were active and 47 (41.6%) were inactive in accordance with PGA. The median ESR was 22 (2–121) mm/h and the median CRP was 2.75 (0–4.1) mg/dL. 47% of patients were on low dose steroids (less than or equal to 5 mg prednisolone or 4 mg methylprednisolone), 19% were on high dose steroids, 76% were on hydroxychloroquine and 57% were on immunosuppressants (16 patients were taking methotrexate, 4 leflunomide, 28 azathioprine, 16 mycophenolate mofetil, 2 cyclophosphamide and 3 rituximab). Patients' clinical features according to the ACR criteria are summarised in Table I.

Anxiety and depression

The mean values (±SD) of HADS-A scores observed in 113 patients and 123 healthy controls were 7.3±4.8 (median; 7, range: 0–20) and 5.7±4.1 (median; 5, range: 0–17) (p=0.001) and HADS-D scores were 6.1±4.7 (median; 5, range: 0–17) and 5.1±3.9 (median; 6, range: 0–18) (p=0.018), respectively.

Of the 113 patients, 19 (16.8%) scored as possible, 18 (15.9%) as probable and 6 (5.3%) as extreme cases of depression and 21 (18.5%) scored as possible, 19 (16.8%) as probable and 12 (10.6%) as extreme cases of anxiety.

When 8 points was taken as the cut-off value, depression was found in 42 (37.2%) cases and in 34 (27.6 %) controls (p=0.042) and anxiety was found in 50 (44.2%) SLE patients and in 24 (19.5%) healthy controls (p=0.02). We used this cut-off value to subdivide SLE population into two groups; patients with HADS score <8 and ≥8 for anxiety and depression and compared these groups with regards to mean SF-36 subscale scores. SLE patients with HADS scores ≥8 had lower HRQoL scores including all domains of SF-36 instrument (p=0.000; for all) when analysed in terms of anxiety and depression (Table III). Patients with anxiety and depression were found to report lower SF-36 scores than the others.

Table I. Clinical characteristics of cases.

Clinical characteristics (ACR criteria)	n, (%)
Malar rash	49 (43.4)
Discoid rash	15 (13.3)
Photosensitivity	75 (66.4)
Oral ulcers	40 (35.4)
Arthritis/arthralgia	80 (70.8)
Serositis	15 (13.3)
Haematological disease	68 (60.2)
Renal disease	42 (37.2)
Central nervous system disease	6 (5.3)
ANA positivity	112 (99.1)
Anti ds-DNA, Sm or phospholipid antibody (+)	61 (54)
SLEDAI (median)(IQR)	2 (0-24)
Physician global assessment (mean) (SD)	0.72±0.71

Disease activity and patient-reported outcomes

Determining the disease activity in consistence with PGA, all of the SF-36 subscale scores, except social functioning (SF) were similar between active and inactive patients. The SF score was 44.66±11.52 in inactive and 39.69±13.94 in active patients (p=0.048) according to PGA (Table III). HADS-A and HADS-D scores were also not statistically different between active and inactive groups [31 (47%) and 19 (40.4%) patients were anxious; p=0.490, 28 (42.4%) and 14 (29.8%) were depressive; p=0.171, respectively]. No correlation was observed between SLEDAI and any of the SF-36 subscales.

HRQoL

The scores of HRQoL, including PCS and MCS of cases *versus* controls were compared in Table II. All SF-36 domain and summary scores were lower in cases than in controls.

Table II. Differences in summary and domain scores of HRQoL between SLE patients and healthy controls.

Characteristics	SLE cases (n=113) mean±SD	Controls (n=123) mean±SD	*p*-value
Global SF-36	41.21 ± 9.00	49.88 ± 6.48	0.000
PCS	40.44 ± 10.55	51.39 ± 9.22	0.000
Physical Function (PF)	43.41 ± 11.36	49.95 ± 7.99	0.000
Role-Physical (RP)	41.11 ± 12.27	50.30 ± 8.44	0.000
Bodily Pain (BP)	42.09 ± 12.18	52.55 ± 9.28	0.000
General Health (GH)	39.53 ± 11.37	50.24 ± 10.23	0.000
MCS	42.01 ± 11.62	48.32 ± 8.37	0.000
Vitality (VT)	44.69 ± 11.10	53.29 ± 8.61	0.000
Social Functioning (SF)	41.76 ± 13.16	50.26 ± 8.37	0.000
Role-Emotional (RE)	40.03 ± 13.12	46.27 ± 9.22	0.000
Mental Health (MH)	40.81 ± 12.80	48.61 ± 10.72	0.000

To determine the relationship between different factors and HRQoL, univariate analyses were performed with the following variables: age, working and marital status, education time, SLEDAI score, depression, anxiety and HRQoL. In linear regression analysis, age was negatively correlated with physical functioning (β= -0.262, *p*=0.005) , bodily pain (β=-0.220, *p*=0.019), general health (β=-0.206, *p*=0.029) and PCS (β=-0.289, *p*=0.002). Years of education positively correlated with bodily pain, general health and PCS (β values were 0.211; 0.220; 0.207, p values were 0.025; 0.019 and 0.028, respectively). No correlation was observed between disease duration, SLEDAI scores and SF-36 subscales.

We also investigated the impact of marital status on HRQoL in our SLE patients. General Health (37.68±10.83, 48.63±10.07; *p*=0.000), vitality (43.16±11.03, 52.62±8.60; *p*=0.001), mental health (39.20±13.22, 48.80±6.96; *p*=0.000), PCS (39.27± 10.27, 40.01±10.36; *p*=0.004) and MCS (41.21±12.18, 46.26±7.98; *p*=0.033) scores were all significantly higher in single patients than married cases. After age adjustment the impact of marital status on SF-36 domains disappeared.

In various studies, employement was found to be an important factor for quality of life in lupus patients so we searched the quality of life parameters also in unemployed and employed patients. Bodily pain (40.47±11.62, 47.50±12.68; *p*=0.009), general health (37.66±10.97, 45.82±10.56; *p*=0.001), vitality (43.07±10.79, 50.13±10.58; *p*=0.004) and PCS (38.82±10.01, 45.89±10.68; *p*=0.002) scores were reported worse by unemployed patients than working ones.

The independent variables that were found significant in univariate analysis were included in the multiple logistic regression models. In multiple logistic regression analyses, the dependent variables, SF-36 subscales, were categorised into two groups; below and above the mean values of patients. After logistic regression analyses, it was found that only HADS-A and HADS-D were significantly associated with most SF-36 subscales. The correlations between other determinants as age, education time, marital status and SF-36 domains were not persistant after multiple logistic regression analysis (Table IV).

Discussion

In this study, we evaluated the impact of age, working status, education time, disease activity, disease duration and mental health on the quality of life in Turkish SLE patients as measured by a general tool, the SF-36. We observed that all domains of SF-36 and physical and mental summary scores were impaired in lupus patients compared with age- and sex-matched healthy controls. Several studies have shown that older age is associated with lower HRQoL scores (19-21). Doria *et al*. also reported that age was one of the major determinants of HRQoL reduction in their lupus cohort (22). In our study, although in univariate analyses age was found significantly related with some SF-36 subscales (mainly physical components), after multivariate analyses these relations disappeared (23, 24).These variances of results may be arising from the differences between the cohorts in terms of patients' different demographical and disease related features.

The relationships between disease duration, education time and marital status with quality of life parameters were also investigated in our study. After logistic regression analysis, the correlations of these determinants' with the SF-36 domain scores disappeared. In some reports, a longer disease duration was found to be associated with better

Table III. SF-36 scores for SLE patients.

	PF	RP	RE	SF	BP	VT	MH	GH	MCS	PCS	Global
HADS-A											
<8	48.15±9.44	45.67±11.87	44.45±11.49	48.16±10.31	47.25±12.21	49.03±11.24	47.05±11.32	45.40±10.0	47.05±9.68	43.68±10.06	46.12±7.55
≥8	37.44±10,81	35.37±10.27	34.45±13.03	33.69±11.94	35.59±8.56	39.23±8.20	32.95±9.97	32.14±8.29	31.68±7.86	33.80±8.25	35.01±6.54
p-value	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
HADS-D											
<8	47.21±9.88	44.38±12.31	42.55±12.57	47.72±9.78	46.40±11.91	49.03±10.28	45.96±10.95	44.47±10.02	47.38±9.18	44.51±9.45	45.39±7.5
≥8	36.99±10.88	35.60±10.14	35.75±13.07	31.68±12.02	34.81±8.78	37.35±8.26	32.10±10.94	37.45±8.26	33.91±10.18	34.30±9.14	34.14±6.61
p-value	0.000	0.000	0.007	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
PGA											
Inactive	44.82±11.29	42.39±12.81	41.41±13.55	44.66±11.52	43.82±10.88	46.67±11.39	42.03±13.92	40.02±11.32	43.64±12.14	41.78±9.07	42.73±8.80
Active	42.42±11.38	40.21±11.89	39.04±12.82	39.69±13.94	40.86±12.97	43.28±10.75	39.94±11.98	39.19±11.47	40.86±11.11	39.50±11.47	40.12±9.05
p-value	0.268	0.353	0.340	0.048	0.204	0.110	0.390	0.703	0.219	0.241	0.129

Table IV. Multivariate logistic regression of variables associated with SF-36 domains.

	Odds ratio	95% CI	*p*-value
Physical Functioning			
HADS-A	3.42	1.23-9.46	0.018
Role Limitation (Physical)			
HADS-A	4.34	1.96-9.64	0.000
Role Limitation (Emotional)			
HADS-A	4.56	2.06-10.13	0.000
Social Functioning			
HADS-A	6.83	1.91-24.32	0.003
HADS-D	4.59	1.09-19.26	0.037
Pain			
HADS-A	4.10	1.45-11.6	0.008
Vitality			
HADS-D	4.18	1.20-14.0	0.024
Mental Health			
HADS-A	18.44	3.99-84.92	0.000
General Health			
HADS-D	11.32	2.59-49.39	0.001
Working Status	0.21	0.05-0.82	0.026
MCS			
HADS-A	25.33	4.45-144.05	0.000
PCS			
HADS-D	6.04	1.71-21.36	0.005
Global SF-36			
HADS-A	25.84	4.51-147.85	0.000

quality of life parameters (4) and in others there was a negative correlation or no associations (22, 25). Working status of patients was associated with general health domain of SF-36 in our lupus cohort. Shen *et al*. reported that socioeconomic factors such as level of education, working status and household income don't have direct influence on HRQoL and they contributed indirectly to quality of life via other factors including depression, anxiety and disease activity (21).

The influence of SLE disease activity on health related quality of life is still a debated issue. We did not find any correlation between disease activity measured by SLEDAI and quality of life, as reported in many other studies (1, 26-28). In contrast with our findings, Shen *et al*. showed that disease activity has both direct and indirect effects on the global SF-36 score in Chinese patients with SLE (21). Doria *et al*. suggested that other determinants, such as anxiety and/or depression, could mask the effects of disease activity on the overall HRQoL in SLE patients with low disease activity as in our study group (22). They reported that the parameters including disease severity, activity and disease related damage could supply us only an incomplete knowledge of the patients' health and it is necessary to search for other aspects as patients' psychopathological state.

It has also shown that SLE patients rate their disease activity according to their psychological status while physicians score lupus activity based on the physical and clinical effects of the disease (29, 30) causing discordance in patients' and physicians' global assessments of disease activity. When we assessed our patients from this point of view, we observed that patients with higher HADS scores have lower HRQoL (Table III). We determined anxiety and depression as the major predicting factors of impaired SF-36 subscales. Moldovan *et al*. reported depression as the major determinant of quality of life in all domains of SF-36 in PATROL study (31). A survey of Chinese SLE patients indicated that both anxiety and depression are substantial predictors of poor HRQoL (21). A literature review of psychosocial research on SLE by Seawell *et al*. demonstrated that psychosocial factors should be considered to understand the disease experience of persons with lupus (32). The results of a study from Republic of Korea showed that quality of life was more influenced by depression and glucocorticoid dose than by disease activity or damage (33). In consistent with these data, it is shown that cognitive-behavioral therapy in SLE patients improves MCS, its components and also physical components of HRQoL (34). In a study from USA, it is shown that patients having little understanding of lupus had higher levels of depression and the authors suggested that support and patient education about lupus may reduce anxious or depressive symptoms of patients (35).

Our study has some limitations. First, it has a cross-sectional nature and the data was collected from only one centre. Secondly, we did not record SLE damage indices of our patients so could not evaluate the influence of disease damage on HRQoL. Thirdly, we did not have information about patients' comorbidities and could not assess the patients for confounding factors such as fatigue or fibromyalgia, which could lead to decrease in HRQoL.

In conclusion, we have shown that HRQoL is not influenced by SLE disease activity and severity directly but clinical and physical signs and symptoms of lupus could lead patients' developing anxiety and/or depression. Psychological status may influence the patients' self-perceived quality of life in a worsenning manner. Based upon these results, HRQoL in SLE patients can not be measured exactly with present measures of disease activity and patients' mental well-being should be taken into consideration. Physicians should pay close attention to detect anxiety and depression and manage them in order to improve quality of life in patients with SLE.

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