



# Mental Health Status and Health-Related Quality of Life among Systemic Lupus Erythematosus (SLE) Patients in Thailand: A Multi-Site Study

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**Background:** The systemic lupus erythematosus (SLE) patients oftentimes suffer from both physical and psychosocial challenges that may lead to low health-related quality of life (HRQoL). However, limited research has been done in this area.

**Objective:** To examine mental health status and HRQoL among SLE patients in Thailand.

**Materials and Methods:** The present study was a cross-sectional study conducted at the rheumatology clinic of four major hospitals in Thailand. The paper-based questionnaire consisted of demographic, health history such as depression, anxiety, stress Scale (DASS-21), and the Rosenberg self-esteem scale (RSE), and the disease-specific Lupus Quality of Life scale (LupusQoL). Depending on the variable's level of measurement such as categorical or continuous, Spearman's Rho or Pearson's product moment correlation coefficients were used to explore the relationships among the variables. Hierarchical multiple regression was used to identify the predictors of LupusQoL.

**Results:** Among the 387 participants, many might have experienced depression, anxiety, and stress (30%, 51%, and 29%, respectively). Self-esteem among the participants was good (31.8 out of 40). All eight domains of LupusQoL were affected with intimate relationship domain being impacted the most. The overall LupusQoL was significantly associated with the number of prescribed medications ( $r=-0.23$ ), depression ( $r=-0.70$ ), anxiety ( $r=-0.58$ ), stress ( $r=-0.67$ ), and self-esteem ( $r=0.59$ ),  $p<0.001$ . Significant predictors of the overall LupusQoL were mental health status (depression, anxiety, and stress) and self-esteem,  $F(3, 81)=43.10$ ,  $p<0.001$ , adjusted  $R^2=0.60$ .

**Conclusion:** SLE patients should be holistically assessed in both physical and psychological aspects. In addition to proper medical treatments, healthcare providers should use a multidisciplinary team approach to resolve the patients' psychosocial issues, which in turn, may increase the patients' quality of life. Self-care education may be necessary to help the patients manage the condition and decrease the number of medications.

**Keywords:** Mental health, Quality of life, SLE, Thailand

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Systemic lupus erythematosus (SLE), an autoimmune disease, affects mostly women between the ages of 15 to 44<sup>(1)</sup>. It is estimated that, at the minimum, five million people worldwide have a form of SLE. The SLE patients suffer from at least one of the disease's various symptoms such as extreme fatigue, painful joints, abnormal blood counts (anemia, low platelets, or low white blood cells), nephritis, cognitive dysfunctions, hair loss, skin rash or butterfly-shaped rash on the face. Currently, SLE remains a life-changing disease with no cure. The lifelong process of treatment focuses on controlling

the symptoms and suppressing the autoimmunity from attacking the patient's body. The most commonly prescribed medications include corticosteroid, antimalarial, and immunosuppressive drugs that also produce a variety of undesirable side effects such as Cushing syndrome, mood changes, insomnia, hair loss, or susceptibility to infectious diseases<sup>(1)</sup>.

While SLE patients are encountering the physical symptoms, they oftentimes struggle to psychosocially adjust and live with the disease. A systemic review and meta-analysis reported high prevalence estimates of depression and anxiety among adult SLE patients at 30% and 40%, respectively<sup>(2)</sup>. The most common causes of depressive or anxious feelings were changes in body appearance and physical limitations. Those with muscle pain and hair loss were the most likely to report depression and anxiety feelings<sup>(3)</sup>. Another study reported that women with SLE had a significant higher perceived stress compared to healthy women<sup>(4)</sup>. In addition, a small study of 40 SLE patients discussed the negative association between self-esteem and having SLE. The disease could strongly impact the physical appearance and emotions, which then might decrease self-esteem<sup>(5)</sup>. A thematic synthesis of qualitative studies also found that SLE patients experienced mental deterioration, prognostic uncertainty, being a burden, hopelessness, fear of rejection, and social stigma<sup>(6)</sup>. These psychosocial issues, in turn, may have an adverse effect, worsening the SLE condition and leading to lower health-related quality of life (HRQoL)<sup>(7)</sup>.

HRQoL is one's perspective of how one's daily function is affected by one's health status<sup>(8)</sup>. When a person develops SLE, the HRQoL is profoundly affected. When using the Medical Outcomes Short Form-36 (SF-36) to measure health status, a study found that the HRQoL in SLE population was lower than in the general population<sup>(9)</sup>. In terms of measuring the HRQoL among SLE patients, SF-36 survey has been criticized of its generic nature<sup>(10)</sup>. While SF-36 allows comparison of the HRQoL in SLE to other health conditions, it may not adequately capture issues that are unique to the disease. To specifically measure the HRQoL among SLE patients, another study used the Lupus Quality of Life questionnaire (LupusQoL) to measure the disease-specific HRQoL among 113 SLE patients. The study found that all domains of LupusQoL were diminished with fatigue domain being impacted the most<sup>(11)</sup>. Furthermore, a recent literature review reported that the lower HRQoL was consistently associated with lower income, lower education, older age, coping skills, comorbidities,

and some clinical manifestations involving the skin, kidneys, muscle, and joints. In addition, since HRQoL was poorly related to disease activities and damage, the review suggested that a comprehensive evaluation of the SLE patients should include HRQoL assessment<sup>(12)</sup>.

As a developing country, Thailand's medical advances have been improving over the past decade. However, it is unclear if the aggressive treatment approach in the past decade increased the SLE patients' quality of life and survival rate. Research evidence has been limited or is somewhat outdated. A study among SLE patients in Thailand reported that the 10-year survival rate was 87%, with the average age at death being 34.1±11.8 years. The most common causes of death were opportunistic pulmonary infections and neuropsychiatric lupus<sup>(13)</sup>. In terms of mental health, only one study has been published. The study reported high rates of depression and anxiety (45.2% and 37.1%) among SLE patients in Thailand. However, the sample size of the present study was small with only 62 SLE patients<sup>(14)</sup>. In addition, evidence of HRQoL among Thai SLE patients was only reported in a single-site study published in 2010. The study used Short Form-36 to assess the general HRQoL of 95 SLE patients. The study reported that all HRQoL domains were impaired and there was no association between HRQoL and the disease<sup>(15)</sup>. Furthermore, there was limited research on disease-specific HRQoL among Thai SLE patients.

To understand the specific needs of SLE patients in Thailand, the present multi-site study aimed to examine the mental health status and disease-specific HRQoL among SLE patients in Thailand. The findings of the present study can be used to tailor interventions or health education programs to better fit the SLE patients' needs.

## Materials and Methods

### Participants and procedures

The present cross-sectional study was conducted at the rheumatology outpatient clinics in four major hospitals, located in the central, eastern, north-eastern, and southern regions of Thailand. The data were collected between January and May 2019. The convenience sample consisted of the patients who were at least 18 years old and had been diagnosed with SLE by an attending physician, using the American College of Rheumatology (ACR) classification criteria for SLE. Qualified patients were approached while they were waiting to see a physician. During the introduction, if the patient was unable to carry on

the conversation because of a history of cognitive or mental impairments according to the medical record, or being too fatigued, the patient was excluded from the study. After reading the informed consent, the patients signed the consent forms if they agreed to participate in the study. The participants then started the survey and might stop or take a break from the survey at any time.

### **Ethical considerations**

The approval to conduct the present study was obtained from each hospital's Institutional Review Board before the data was collected (Approval #MURA2018/918, 032/2561, EC 58/2561, and REC 61-325-14-1, respectively). The participants' consent forms were obtained before data collection.

### **Measures**

Variables of interest to the present study included demographic characteristics, health history, mental health status such as depression, anxiety, and stress, self-esteem, and SLE-related quality of life. The paper-based survey comprised of four parts, 1) demographic and health history, 2) Depression, Anxiety, Stress Scale (DASS-21)-Thai version, 3) Rosenberg Self-Esteem Scale, and 4) LupusQoL Scale. Demographic and health history included age, gender, religion, education level, employment, income, relationship status, age when diagnosed with SLE, and the number of current medications. DASS-21-Thai version contained three self-reported scales designed to measure depression, anxiety, and stress. Each scale contained seven rating statements. Participants rated each statement from 0 (did not apply to me at all) to 3 (applied to me very much or most of the time) based on their feelings or psychological symptoms they had in the past week. The possible range of score for each scale was 0 to 21<sup>(16)</sup>. The Cronbach's alpha for each scale was good, ranging from 0.78 to 0.85.

Rosenberg self-esteem scale (RSE)-Thai version contained 10 Likert-scale statements. The participants must choose how much they agreed with each statement from 1 (strongly disagree) to 4 (strongly agree). The possible range of RSE scale was from 10 to 40. The higher the score, the higher the self-esteem level<sup>(17)</sup>. The Cronbach's alpha was 0.78.

LupusQoL Scale-Thai version is a disease-specific, HRQoL questionnaire that has been used widely and translated into various languages<sup>(18)</sup>. LupusQoL has gone through the most validation process and would be most appropriate for cross-

sectional measurement of HRQoL<sup>(10)</sup>. The LupusQoL scale contained 34 SLE-associated physical, emotional, and social items that the participants must rate how often they experienced in the past four weeks with 0 (always) to 4 (not at all). The scale was grouped into eight domains. Each domain's average score was divided by 4 and multiplied by 100 to get the transformed score, ranging from 0 (worst HRQoL) to 100 (best HRQoL)<sup>(18)</sup>. The Cronbach's alphas for seven out of eight domains was good, and were physical health (eight items, 0.85), pain (three items, 0.83), planning (three items, 0.88), intimate relationship (two items, 0.93), burden to others (three items, 0.89), emotional health (six items, 0.92), and body image (five items, 0.90). For fatigue domain (four items), the Cronbach's alpha was 0.67. After the statement #33 "I have to go to bed early because of my lupus" was deleted, the Cronbach's alpha was 0.77.

### **Statistical analysis**

The study data were analyzed via Statistical Package for the Social Sciences (SPSS) program. Descriptive statistics were used to present basic demographic, health history, mental health status, self-esteem, and HRQoL. Spearman's Rho correlation coefficients were used to identify the association between nominal or categorical variables and the variables of interest such as mental health status, self-esteem, and HRQoL. Pearson's product moment correlation coefficients were used to identify the association between continuous variables and the variables of interest. Hierarchical multiple regression was used to explore the predictors of the quality of life. At least 59 subjects were required to use a multiple regression analysis with the statistical parameters of the power at 0.9, effect size at 0.15, alpha at 0.05, and three significantly-related predictors, the number of prescribed medications, DASS, and RSE<sup>(19)</sup>.

## **Results**

### **Demographic and health history**

Three hundred ninety-one participants agreed to participate in the survey. However, four had more than 20% missing data. Thus, only 387 participants were included in the data analyses.

Out of 387 participants, most were females and Buddhist. About half (52.0%) had high school diploma or lower. Approximately one-fifth of the participants were not-employed (20.0%) and did not have enough income for living expenses (23.0%). The participants' average age was 40 years old and they had been living with SLE for 10 years. On the average,

**Table 1.** Demographic and health history of the participants

Variables	Frequencies (%)
Sex (n=387)	
Female	369 (95.3)
Male	18 (4.7)
Religion (n=387)	
Buddhists	351 (90.7)
Non-Buddhists	36 (9.3)
Education (n=387)	
Middle school or below	116 (30.0)
High school	85 (22.0)
Associate degree	46 (11.9)
Bachelor's degree	115 (29.7)
Master's degree or higher	25 (6.4)
Income (n=282)	
Not sufficient	65 (23.1)
Sufficient	171 (60.6)
More than sufficient	46 (16.3)
Relationship Status (n=387)	
Single	108 (27.9)
Dating	47 (12.1)
Married	191 (49.4)
Other (separated, divorced, widowed)	41 (10.6)
Employment (n=384)	
Not employed	77 (20.0)
Students	23 (6.0)
Employed	284 (74.0)
Age (n=385); mean±SD	
Min-max	18 to 77
Age when diagnosed with SLE (n=277); mean±SD	
Min-max	2 to 76
No. of years having SLE (n=277); mean±SD	
Min-max	0 to 50
No. of prescribed medications (n=146); mean±SD	
Min-max	1 to 16

SLE=systemic lupus erythematosus; SD=standard deviation

each participant had six prescribed medications for their SLE conditions (Table 1).

### Mental health status (DASS)

The mean score for depression was 3.6 (SD 3.7). When using the DASS recommended cut-off scores to categorize the severity of depression<sup>(16)</sup>, this average depression score was considered as normal. However, when reviewing individual scores, it was found

that 29.9% of the participants were categorized as having mild to extremely severe level of depression. The mean score for anxiety was 4.5 (SD 3.7), which was categorized as mild anxiety. Over half of the participants (51.4%) might have experienced mild to extremely severe level of anxiety. The mean score for stress was 5.8 (SD 4.1), which was categorized as normal. However, 29.7% of the participants might have experienced mild to extremely severe level of stress (Table 2).

### Self-esteem (RSE)

Out of 378 participants who completed all RSE items, the mean RSE score was 31.8 (SD 4.1, min 20, max 40).

### Correlations between mental health, demographic, and health history

As shown in Table 3, low correlations were found among the variables of interest. Higher depression level was related to the higher number of prescribed medications ( $r=0.22$ ), and lower income ( $r=-0.19$ ). Higher anxiety level was associated with younger age ( $r=-0.10$ ), earlier age when diagnosed ( $r=-0.15$ ), and the higher number of prescribed medication ( $r=0.17$ ). Higher stress level was correlated with earlier age when diagnosed ( $r=-0.17$ ), the higher number of years having SLE ( $r=0.14$ ), and lower income ( $r=-0.12$ ). Higher self-esteem level was related to higher income ( $r=0.21$ ) and higher education ( $r=0.13$ ).

The present study also found that self-esteem was moderately associated with depression ( $r=-0.55$ ), anxiety ( $r=-0.41$ ), and stress ( $r=-0.46$ ),  $p<0.001$ . In addition, the correlations between depression, anxiety, and stress were strong ( $r=0.72$  to  $0.76$ ,  $p<0.001$ ). The high correlations support the idea that these three variables were intertwined<sup>(20)</sup>.

### Health-related quality of life (LupusQoL)

All eight domains of the LupusQoL were impaired. The most affected domains included intimate relationship (61.3 out of 100), body image (76.4 out of 100), and burden to others (76.5 out of 100). Low correlations were found among the LupusQoL domains and the variables of interest. Younger age, earlier age when diagnosed with SLE, less prescribed medications, higher income, and being employed were significantly related to at least one of the LupusQoL domains. When looking at LupusQoL total, the smaller number of prescribed medications was associated with better overall LupusQoL (Table 4).

**Table 2.** Mental health status (depression, anxiety, and stress) among SLE patients

Variables/severity	Normal	Mild	Moderate	Severe	Extremely severe
Depression (n=381)	71.1%	12.1%	11.8%	2.6%	2.4%
Mean 3.6, SD 3.7, min-max 0 to 21					
Anxiety (n=381)	48.6%	11.5%	20.2%	10.8%	8.8%
Mean 4.5, SD 3.7, min-max 0 to 18					
Stress (n=380)	70.3%	13.4%	9.2%	5.1%	2.1%
Mean 5.8, SD 4.1, min-max 0 to 21					

SD=standard deviation

**Table 3.** Correlations between mental health status, demographic, and health history

Variables	Age	Age when diagnosed	No. of prescribed medications	No. of years having SLE	Income	Education
Depression	-0.07	-0.11	0.22*	0.06	-0.19**	-0.05
Anxiety	-0.10*	-0.15*	0.17*	0.06	-0.11	0.04
Stress	-0.06	-0.17**	0.02	0.14*	-0.12*	0.01
Self-esteem	0.03	0.02	0.05	0.01	0.21**	0.13*

SLE=systemic lupus erythematosus  
\* p<0.05, \*\* p<0.01

**Table 4.** Significant correlations between LupusQoL and demographic/health history

QoL domains	Mean (SD)	Age	Age when diagnosed	No. of prescribed medications	Income	Employment
Physical health	80.6 (17.6)	-0.14**	-0.17**	-0.19*	0.22**	0.16**
Pain	81.7 (19.3)	-0.07	-0.03	-0.09	0.20**	0.07
Plan	80.6 (21.6)	-0.09	-0.12*	-0.09	0.13*	0.14**
Intimate relationship	61.3 (33.1)	-0.27**	-0.29**	-0.12	0.03	0.11
Burden to others	76.5 (21.7)	0.15**	0.04	-0.09	0.15*	0.07
Emotion	81.3 (16.3)	0.10*	0.07	-0.16	0.08	0.05
Body image	76.4 (22.3)	0.16*	0.11	-0.03	0.07	0.08
Fatigue	79.5 (18.1)	0.08	0.09	-0.11	0.07	0.01
LupusQoL total	76.9 (16.5)	0.00	0.08	-0.23*	0.14	0.07

LupusQoL=Lupus quality of life scale; SD=standard deviation  
\* p<0.05, \*\* p<0.01

The LupusQoL total score was highly negatively related to depression ( $r=-0.70$ ), anxiety ( $r=-0.58$ ), and stress ( $r=-0.67$ ), but positively related to self-esteem ( $r=0.59$ ),  $p<0.001$ . When checking the assumptions of using multiple regression analysis, high correlations among depression, anxiety, and stress were found ( $r=0.72$  to  $0.76$ ). Multicollinearity was also noted. To achieve reliable prediction model, these three variables were combined as “mental health status” variable because they were theoretically intertwined mental health issues<sup>(20)</sup>.

To examine how well mental health status and

self-esteem predict LupusQoL total score, when controlling for the number of prescribed medications, a hierarchical multiple regression was computed. When the number of prescribed medications was entered alone, it significantly predicted LupusQoL total,  $F(1, 83)=5.40$ ,  $p<0.05$ , adjusted  $R^2=0.05$ . However, as shown by the  $R^2$ , only 5% of the variance in LupusQoL could be predicted by the number of medications. When the mental health status and self-esteem variables were added, they significantly increased the predictability ( $R^2$ -change=0.55). Those three variables significantly predicted the LupusQoL

**Table 5.** Hierarchical multiple regression analysis summary for mental health status and self-esteem, controlling the number of prescribed medications variable, predicting LupusQoL total

Variables	B	SEB	$\beta$	R <sup>2</sup>	$\Delta R^2$
Step 1					
No. of prescribed medications	-1.64	0.70	-0.25*	0.06	0.06
Constant	88.75	4.75			
Step 2					
No. of prescribed medications	-0.90	0.47	-1.93	0.62	0.55
Mental health	-0.76	0.13	-0.52**		
Self-esteem	1.21	0.34	0.31**		
Constant	55.57	12.28			

\* p<0.05, \*\* p<0.01

total,  $F(3, 81) = 43.10$ ,  $p < 0.001$ , adjusted  $R^2 = 0.60$ , meaning 60% of the variance in LupusQoL total could be predicted by the number of prescribed medications, mental health status, and self-esteem. However, only mental health status and self-esteem were significantly contributing to the model (Table 5).

## Discussion

Similar to the U.S. statistics<sup>(1)</sup>, the present study found that most SLE patients were female and most were diagnosed with SLE during their reproductive years. A retrospective study reviewing 749 Thai SLE patient charts between 1996 and 2005 reported the average age of death was 34 years and the disease duration among the survivals was seven years<sup>(13)</sup>. Encouragingly, the SLE patients in the present study already lived longer (the mean age of 40 years) and, on average, had been living with SLE for 10 years.

### Mental health

The present study found a great number of SLE patients were facing psychological challenges. Similar to a previous study<sup>(14)</sup>, approximately 30% of the patients were categorized as having depression. This number was much higher than the 11.5% mild to severe depression prevalence rate among adults who visited the outpatient clinics in Thailand<sup>(21)</sup>. This high depression rate could be from the autoimmune attacking the central nervous system, causing depression, and could also be a psychological outcome of SLE illness<sup>(22,23)</sup>.

Furthermore, 51.4% of the patients were categorized as having anxiety. A meta-analysis, using 59 qualified studies conducted in America, Asia, Europe, Africa, and Oceania also reported the anxiety prevalence to be 40%<sup>(2)</sup>. While keeping in mind that

corticosteroids, a commonly used drug among SLE patients, could cause some side effects that mimic anxiety symptoms<sup>(24)</sup>, the high percentage of anxiety could not be ignored. Intertwining with depression and anxiety, the prevalence of stress was also at 29%. The high stress level might negatively impact the patient's anxiety, depression, and physical well-being leading to a lower quality of life<sup>(4,25)</sup>.

The present study found higher levels of depression and anxiety were associated with higher number of prescribed medications. To successfully control SLE conditions, health care providers must provide proper treatments as well as self-care education to patients. When SLE is under control, fewer medications will be needed, which may help decrease depression and anxiety as well. The SLE patients with depression or anxiety should also be referred for psychiatric treatment or psychotherapy so that they can cope with the psychological challenges.

For self-esteem (the person's positive or negative attitude toward themselves as a whole<sup>(26)</sup>), the present study found that the SLE participants had good self-esteem level (31.8 out of 40) and self-esteem was negatively associated with depression, anxiety, and stress level. Consistent with previous studies, self-esteem could not predict one's performance in areas such as job, study, or relationship with others, but it had a positive relation to happiness and a negative relation to depression<sup>(26,27)</sup>. Furthermore, similarly to previous studies<sup>(28,29)</sup>, self-esteem was positively associated with income and education level. Patients who are unemployed or do not have sufficient income should be referred to a social worker. Helping the unemployed patients earn income through job skill training or further education may increase their self-esteem and decrease stress levels.

## Quality of life

It has been known that SLE patients had lower HRQoL when compared to the general populations<sup>(9)</sup>. When examining for the disease-specific HRQoL, the present study found that all eight domains of the quality of life were impaired. The most affected domains were intimate relationship, body image, and burden to the others. These results were similar to previous studies conducted in Turkey and Mexico<sup>(11,30)</sup>.

In Thai society, discussing sex with a partner may be viewed as “improper” since sex education or discussion has been restricted in both school and family settings<sup>(31)</sup>. As shown in the present study, in addition to the physical limitations, the older patients might have a harder time dealing with intimate relationship issues because of the societal restriction. However, if the patients were diagnosed at a younger age, they might have adjusted to the condition through time and were able to continue the intimate relationship with their partners. Health care providers should assess the patient’s intimate relationship status and, when appropriate, refer the patient and partner to family counselling.

The present study found a positive correlation between body image and age. Younger patients felt more impact of the disease on their body image. This could be due to their own maturity level combined with ominous advertisement regarding external beauty in Thailand<sup>(32)</sup>. Connecting patients with an SLE support group who share similar issues such as butterfly-rash, hair loss, gain weight, or rounded face may alleviate the body image concerns. Gaining positive body image may in turn increase self-esteem and decrease depression<sup>(32,33)</sup>.

Furthermore, the present study found that the SLE patients who were older and had more income felt less burden to others. In addition to equipping patients with job skills, health care providers must actively advocate for a better health policy. For example, the Thai government should at least subsidize the cost of the expensive, but critically needed SLE medications that are not covered under the current universal healthcare system<sup>(34)</sup>.

Consistent with previous studies<sup>(35-37)</sup>, patients with serious mental health problems and low self-esteem likely would have low HRQoL. It is critical for health care professionals to use a holistic approach to care for patients with this complicated disease. Patient assessment must cover both physical and psychosocial aspects. The interventions need to be comprehensive. Medications alone may not increase the patient’s

quality of life. A multidiscipline team approach from physician, pharmacist, nurse, psychologist, and social worker is required to meet the goal of helping SLE patients control the disease and have good quality of life.

## Limitation

The study provided informative findings that health care providers may apply to the SLE patients in Thailand. However, it had some limitations. The present study used a convenient sample. The generalizability of the finding may be limited. Recalling bias might cause self-reporting errors. In addition, the study did not examine the relationship between the quality of life and SLE disease activities and damage. Previously, the finding in this area has been inconsistent. One study found no significant association between the quality of life and the disease activity<sup>(11)</sup>. On a contrary, two studies reported the significant association between the disease activity state and quality of life<sup>(38,39)</sup>. In addition, the present study did not explore the organ involvement, comorbidities, and cognitive impairment variables. These variables should be included in the future research. Furthermore, a pilot study should be conducted to examine if a holistic-approach intervention program would enhance the SLE patients’ mental health and HRQoL. Lastly, if time and funding allowed, a longitudinal study to confirm causal relationships between the mental health issues and quality of life should be conducted.

## What is already known on this topic?

Previous studies from other countries reported SLE patients have experienced more mental health issues and lower quality of life, compared to the general population.

## What this study adds?

This study was the first multi-site study in Thailand that examined the mental health and disease-specific quality of life among the SLE patients. This study identified the significant factors influencing the quality of life such as mental health including depression, anxiety, and stress, and self-esteem.

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### Conflicts of interest

The authors report no conflict of interest with respect to the research, authorship, or publication of this article.

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