Prevalence and biopsychosocial factors associated with depressive symptoms among patients living with systemic lupus erythematosus in clinical settings in urban Thailand

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Abstract

Background

Depressive symptoms are globally recognized as a significant mental health problem in patients with chronic disease, particularly those with systemic lupus erythematosus (SLE). The purpose of this study was to estimate the prevalence and examine biopsychosocial factors of depressive symptoms among patients with SLE.

Methods

This cross-sectional study was conducted among 185 participants diagnosed with SLE and received treatment for at least three months, aged 18-59 years attending the outpatient clinic of a university hospital, Bangkok, Thailand. Depressive symptoms were measured by the Thai version of the Patient Health Questionnaire-9 (PHQ-9). We assessed Demographic data, the Systemic Lupus Erythematosus Activity Index (SLEDAI), the Systemic Lupus International Collaborating Clinics Damage Index (SLICC Damage Index), Numeric Rating Scale (NRS), Fatigue Severity Scale (FSS), Body Image Scale (BIS), and the ENRICH Social Support Instrument (ESSI). Data were collected from March to May 2021. Multivariable logistic regression was used to analyze the data.

Result

The proportion of the participants with depressive symptoms was 43.2%, while 8.1% of those patients faced moderate to severe depressive symptoms and could be diagnosed with depression. SLE patients with depressive symptoms were more likely to be severe pain (aOR = 12.11, 95%CI = 1.35-108.46), fatigue (aOR = 2.36, 95%CI = 1.08-5.14), taking prednisolone ≥ 15 mg daily (aOR = 5.75, 95%CI = 1.76-18.80), low satisfied of body image (aOR = 12.49, 95%CI = 2.23-69.80), and low social support (aOR = 17.96, 95% CI = 1.86-173.77). Disease flare, organ damage, and family income sufficiency could not predict the risk of depressive symptoms in patients with SLE ($p \leq .05$).

Conclusion

The findings highlight depressive symptoms in patients with SLE. Therefore, the health professional should be concerned about the perception of body image, level of social support, fatigue, and pain while treating patients with SLE. Public health screening programs to identify depressive symptoms in patients with SLE are needed. In addition, a high dose of prednisolone should be considered if required, along with monitoring.

Introduction

Depression is the most frequent among neuropsychiatric complaints in patients with Systemic Lupus Erythematosus (SLE) (1, 2). Point prevalence rates range from 2 to 91.7%, depending upon the context, setting, and assessment tool (2, 3). While 8 to 24% of patients could be diagnosed with depressive disorders (3, 4), and induce 12% of suicidal thoughts (5). A previous study in northern Thailand revealed that the prevalence of depressive symptoms among patients with SLE was 45.2% (6). Depression is the most frequent and profoundly impactful comorbidity for SLE patients' health and well-being (7), of which depression is a common manifestation, with higher levels of fatigue, more significant pain, and poor sleep quality (8, 9, 10), including increased suicide ideation (5). The associated factors with depression in patients with SLE are controversial (2). Clinical factors related to disease activities, psychobiological factors, and psychosocial factors were hypothesized as factors that might underline the plausibility of associations. The biological, psychological, and social predictors of depression among patients with SLE are rarely reported simultaneously.

SLE is the prototypical autoimmune disease affecting multi-organ systems. A complex interaction of genetics, environment, and hormones leads to immune dysregulation and breakdown of tolerance to self-antigens, resulting in autoantibody production, inflammation, and destruction of end-organs. It is a significant disease burden across the world among different ethnic, racial, and age groups (11). SLE is troubling 1 to 12 people per 5000 worldwide (12), and the incidence of the disease was 0.9 to 3.1 cases per 100,000 populations per year (13). Usually, patients with SLE are first diagnosed in early adulthood. Most cases of this disease are found in 80 to 90% of females between the ages of 20 and 40 years (mean age at diagnosis: 29 years) (14), and it is more common in Afro-Caribbean, Chinese and Asian populations compared with Whites (15).

The nature of SLE is a complex disease that can affect the body without limitation, and the disease causes many different clinical symptoms (14). Typically patients with SLE have an inflammatory illness that occurs in various organ systems and complications from treatments. At the same time, patients with this disease need treatment with long-term monitoring of symptoms since the diagnosis of SLE is more accurate nowadays. The treatment of this disease emphasizes the adjustment of the level of the drug per the results of biomarkers and disease manifestations, as well as impacts of SLE signaling appropriate treatment recommendations. However, one treatment may not continuously address the patient's overall health condition due to the generalized and chronic nature of the disease. This state has long-term effects, with significant impacts on physical and mental health, including the patient's quality of life (14). A previous study reported that more than 2 out of 3 patients with SLE experience emotional illness such as sadness, depression, fear, anxiety, guilt, anger, and wrath (14). These morbidities may seriously affect their ability, leading to significant psychological problems (5).

Depressive symptoms are the most common psychological symptoms complaint in patients with SLE (2). A study found that 24% of patients with SLE were diagnosed together with major depressive disorder (4). Depressive symptoms can intensify pain, as well as fatigue, insomnia, and sluggishness (16). At the same time, it limits a person's physical performance and ability to interact with others (16). In addition, the burden of SLE comorbid with depression may increase the risk of suicide (17). A study found that

depression was associated with disease activity, and SLE disease activity might reveal the covert damage of the central nervous system in SLE (3). Biopsychosocial factors that are critical and related to the depressive symptoms of patients with SLE are presented in figure 1.

Malfunction and injuries in various body organs are essential factors that cause patients to face grave disease prognoses. The severity of SLE, including active disease or disease flare and disability of organ damage (21, 22), and pain suffering and fatigue increase the risk of depressive symptoms (19). Changes in physiology and the immune system are common in patients with SLE. Patients with SLE fear the disease progression, another aggravation or spreading to new organs, and insecurity regarding one's future life. It is often related to unpleasant experiences (14, 20). Fatigue and pain are also common symptoms in SLE; 50 to 90% of patients with SLE experience constant fatigue (14), and over 90% of patients with SLE suffer from joint pain (14, 23). These problems cause patients to struggle with fatigue as paralyzing, insurmountable with sleep or rest. It limits everyday activities, often forcing patients to resign from earlier interests, hobbies, or work. Sometimes, patients feel helpless, powerless, angry, and guilty. Therefore, fatigue and pain were the two most reported symptoms affecting patients' quality of life with SLE, limiting everyday life activities (24). According to the studies, fatigue was a significant contributor to depression in patients with SLE (19), and over 82% of these patients with depressive symptoms experience moderate to severe pain (25).

Patients with SLE are often treated with glucocorticoids as monotherapy or in combination with hydroxychloroquine, NSAIDs, and immunosuppressants. Studies show that immunosuppressants (methotrexate, cyclophosphamide) reduce disease activity (26). However, the unpleasant side effects of high doses of steroid therapy can cause symptoms of neuropsychiatric lupus but more often cause milder emotional changes, such as anxiety or depression. The studies found that taking prednisolone doses more than 15 to 40 mg per day was a factor that could predict depression in patients with SLE (21, 27).

Changing physical appearance from disease progression and its treatment leads to low self-esteem and increases the risk of depressive symptoms (28, 29). Unsightly skin lesions such as classic erythema on the face, discoid rash, lesions with a tendency to scarring, skin atrophy, and hair loss are symptoms that cause patients with SLE to feel embarrassed. Patients also report bruising susceptibility and increased photosensitivity. In addition, the side effect of glucocorticosteroid medicine also is a cause of unsightly skin lesions and obesity (23). This appearance change may make patients feel less attractive and cause concern about adverse reactions from their partners (23). As a result, many patients tend to lose confidence and have lower satisfaction with their self-image.

Living with SLE hurts partnerships, family relationships, and social life. Due to increasing disability, the patients spend less quality time and diminished time with their partners (25). The unpredictable course of SLE is the reason why patients' social life is limited. It frustrates them, fear rejection, and increases their isolation. Patients with SLE who lack good social support often face conflicts with family members that

cause mental health problems, particularly depressive symptoms (22). On the contrary, relevant support ensured by the family or close persons makes it possible for the patients to avoid excessive burden (18).

Poor financial status or insufficiency of household income is a factor associated with depressive symptoms in patients with SLE (30). After five years with SLE, 15 to 40% of patients had lost their jobs. After 10 or 15 years, this percentage increased to 36% and 52%, respectively (14, 31). Many patients with SLE are distressed that the disease will adversely affect their planned development path (14). The patients are also concerned about illness costs, such as medical and additional healthcare insurance costs (24).

Previous studies about depressive symptoms in patients with SLE have mainly been conducted in Western ethnic patients that may influence the results of these studies. Genetics, characteristics, beliefs, cultures, and lifestyles of patients in the East, including Thais, may have different effects (32). In addition, most studies focused on analyzing only the psychological factors (2). The analysis of biopsychosocial factors simultaneously was rare. The results are not sufficiently conclusive for clinical application.

The present study aimed to analyze the prevalence of depressive symptoms and determine biopsychosocial factors associated with depressive symptoms among patients living with SLE in clinical settings in urban Thailand.

This study used the conceptual framework of the Biopsychosocial model (BPS) by George Libman Engel (33) (Figure 1). Therefore, the analysis of comprehensive factors can further develop interventions to prevent mental health problems in patients with SLE and encourage them to live healthy lives.

Methods

A cross-sectional study was conducted in three outpatient medical clinics, including the medicine, nephrology, and rheumatology clinics of a university hospital in Bangkok, Thailand.

Setting

Thailand is an upper-middle-income country located in South-East Asia. The current population of Thailand is 70,005,912 based on Worldometer elaboration of the latest United Nations data (34). 51.1% of the population is urban, most of the population are adults, and the average median age is 40.1 years (34). The National Statistical Office of Thailand (NSO) reported that more than 1 in 5 of Thailand's population health has some chronic illness or congenital disease (35). Most of the Thai population has government health care benefits. Most use universal health insurance (gold card), followed by the social security scheme, civil servant scheme, or state enterprises scheme. The research was conducted at a university hospital established in 1914 in Bangkok city, the capital of Thailand. The hospital is a tertiary hospital governed by the Thai Red Cross Society and affiliated with the faculty of medicine with inpatient services of 1,435 beds. This hospital is a training institute in physical health and mental health for expertise in health professionals and readiness of medical devices for complex illness. A total number of

patients with SLE (ICD-10: M32) by information technology data management of the hospital in 2019 to 2020 reported that more than 1,098 patients with SLE were admitted to the outpatient department. They will get a physical exam, standard treatment, and assessment by division of rheumatology from specialists. Patients with SLE enrolled in the study will be followed up at the outpatient department in one out of three clinics, including internal medicine, kidney, and rheumatology clinics.

Data collection operations took place during the covid-19 outbreak. The researcher and participants strictly complied with the rules for preventing the spread of infection by completing questionnaires and body temperature checks, always wearing masks, and keeping social distancing of at least 2 meters.

Participants

Patients with SLE were recruited at the time of their routine follow-up visit. The patients were eligible if they had aged between 18 and 59 years old, met the revised American College of Rheumatology (ACR) classification, and were on medication for at least three months. All patients were from Thai population and ability to understand Thai and give informed consent in the Thai language. However, those who were unable to provide essential information required in the study protocol, lack of the necessary communication skills, diagnosed with psychiatric disorders, severe physical illness, or in need of urgent treatment were excluded from the study.

The sample size was calculated by G*Power version 3.1.9.7 program and based on the results of a study, an independent pain variable by Chang et al. (2015) (30) depression and quality of life in patients with systemic lupus erythematosus: odd = 3.477, two tails x distribution equal to the binomial, confidence level in test $\alpha = 0.05$, power of test = 0.80, relationship between other variables (R^2 other X) = 0, and X parm $\pi = 0.638$, at least 168 participants were needed. Adding 10.0% to account for error during the study, at least 185 participants were required for the analysis.

Instruments

The socio-demographic and medical history questionnaire was developed by researchers and consisted of 19 items divided into two parts:

Part 1: Personal information contains items about sex, age, religion, marital status, education level, occupation, rights to medical treatment, family characteristics, number of family members, average family income per month, and the sufficiency of household income.

Part 2: Clinical information contains items about the duration of SLE disease, daily steroid dosage, disease flare, other congenital diseases, history of mental illness, weight, height, and body mass index.

Assessment of depressive symptoms

Depressive symptoms were evaluated with the Thai version of the nine-item Patient Health Questionnaire (PHQ-9) (36). The Thai version of the PHQ-9 was translated from the original PHQ-9 (37). The PHQ-9 is a self-report measure consisting of 9 questions based on the 9 DSM-IV criteria for major depressive

episodes. The respondents rated the symptoms experienced during the prior two weeks. Scores for each item range from 0 (not at all) to 1 (several days), 2 (more than half of the days), and 3 (nearly every day), while summed scores range from 0 to 27. The total scores were classified as indicating the level of severity of depressive symptoms: mild (5 to 9), moderate (10 to 14), moderately severe (15 to 19), and severe depression (20 and over). The Thai version of the PHQ-9 has acceptable psychometric properties for screening for major depression in general practice with a recommended cut-off score of nine or greater. Cronbach's alpha for the total scale was 0.79, and predictive validity was 0.96 (36).

Measures of biological predictors

The Systemic Lupus Erythematosus Activity Index (SLEDAI), developed by Bombardier et al. (1992), was used to assess disease flare (38). This instrument collected data from participants' medical records by the researcher that was trained by a nephrologist. The SLEDAI consists of 24 questions about symptoms and laboratory results. The answer characteristic is a rating scale ranging from 1, 2, 4, and 8 points. In this study, disease flare was divided into two groups: the non-disease flare group, which scored less than 3 points, and the disease flare group, three or higher.

The Systemic Lupus International Collaborating Clinics Damage Index (SLICC Damage Index) developed by Gladman et al. (1996) was used to assess organ damage (39). The SLICC damage index consists of 12 questions about damage to 12 organ systems in the body. The answer characteristic is a rating scale ranging from 1 to 2 points. In this study, organ damage was divided into two groups: the non-organ damaged group: 0 points, and the group with organ damage: the score was 1 point or higher. This instrument collected data from participants' medical records by the researcher that was trained by a nephrologist.

Numeric Rating Scale (NRS) was used to measure pain scale, developed by Jensen & Karoly (2001) (40) and updated by the Thai association for the study of pain (2009). The NRS consists of 1 question about the position of pain and the pain measurement. The answer characteristic is a numeric scale with a score of 0 to 10. In this study, the pain was divided into four groups: the group with no pain: the score was 0 points, the group with mild pain: the score was 1 to 3 points, the group with moderate pain: the score was 4 to 6 points, and the group with severe pain: the score was 7 points or higher. The pain assessment was adjusted by self-report of participants.

Fatigue Severity Scale (FSS) was used to measure fatigue severity; it was developed by Krupp et al. (1989) (41) and translated into a Thai version by Auayporn Sawasdee (2014). The FSS consists of 9 questions, eight levels of Likert scale from 1 to 7 points. The score is calculated based on the points from the answers divided by the total number of questions. In this study, fatigue was split into two groups: the group without fatigue: the score was less than 4 points, and the fatigue group was 4 points or higher. Content validity with three panel experts yielded a CVI score of 1. The internal consistency in those living with SLE (n=30) obtained a Cronbach's alpha coefficient of .89. The fatigue assessment was adjusted by self-report of participants.

Measures of psychological predictors

Body Image Scale (BIS) was used to measure the level of body-image satisfaction as developed by Hopwood et al. (2001) (42) and translated into Thai version by Bencharat Cheewapoonpol (2004). The BIS consists of 10 negative questions about satisfaction with their physical image. The answer is a rating scale of 4 levels from 1 to 4 points. In this study, there were three groups of physical image satisfaction groups: the group with low level: the score was 31 to 40 points, the group with moderate level: the score was 21 to 30 points, and the group with high level: the score was 10 to 20 points. Content validity rated by a panel of three experts yielded a CVI score of 1. The internal consistency in those living with SLE (n=30) obtained a Cronbach's alpha coefficient of .89. The body image assessment was adjusted by self-report of participants.

Measure Of Social Predictor

The ENRICHD Social Support Instrument (ESSI) was used to measure social support, developed by Mitchell et al. (2003) (43) and translated into Thai version by Chantana Lootjanakul (2006). The ESSI consists of 7 questions. The answer is a rating scale of 5 levels from 1 to 5 points. In this study, there were two groups of social support: the group with mild social support: the score was 1 to 10 points, the group with moderate social support: the score was 11 to 20 points, and the group with high social support: the score was 21 to 30 points. Content validity with three panel experts yielded a CVI score of .95. The internal consistency in those living with SLE (n=30) obtained a Cronbach's alpha coefficient of .94. The social support assessment was adjusted by self-report of participants.

Ethical Consideration

Ethical approval

was granted by the Institutional Review Board Faculty of Nursing, Mahidol University (IRB-NS2020/42.3010), and the Institutional Review Board Faculty of Medicine, Chulalongkorn University, Thailand (IRB No. 099/64). In addition, the committee for research of the hospital approved the research project before working with human subjects. Participants completed informed consent forms. The researcher also asked subjects' permission to use the data contained in their medical records. All procedures were performed in accordance with the Declaration of Helsinki, The Belmont Report, CIOMS guideline and International Conference on Harmonization in Good Clinical Practice (ICH-GCP). The study was conducted from November 2020 through July 2021, and participant recruitment was active from March 2021 through May 2021. The participants answered six questionnaires by themselves, including 48 questions, the data collection produced approximately 20 to 25 minutes for each participant.

Data analysis

Data were double entered into an Excel sheet before being transferred into the SPSS program version 22.0 for analysis. Categorical and continuous data were appropriately analyzed to present the

characteristics of participants by descriptive statistics. The chi-square test was used to assess characteristics between patients with and without depressive symptoms. Univariable logistic regression analysis was performed per each biopsychosocial variable. The complete multivariable logistic regression analysis model included all significant independent variables at a significance level of $\alpha = 0.05$.

Results

Personal characteristics of the participants

The study comprised 185 Thai men and women who were diagnosed with SLE. Most of them were female (96.2%), between 36 and 59 years old (70.3%), with an average age of 42.16 years old (SD = 10.78), single (52.4%), Buddhists (95.7%), and hold bachelor's degree (42.7%). Most of the patients work (72%) and use the social security schemes to access healthcare (38.9%). Most of the patients are dwelling in single families (81.1%) with 1 to 3 of family members (57.8%), the average household monthly incomes were between 10,000 and 25,000 baht (34.1%) and had no income leftover (51.4%) (Table 1).

Clinical Characteristics Of The Participants

Most of the patients had been diagnosed with SLE for 11 to 20 years (36.8%), took prednisolone 1 to 5 mg daily (48.1%), and had disease remission (78.4%). The result showed that 161 (87% of patients) had other congenital diseases, for instance, lupus nephritis (47%), hypertension (19.5%), and dyslipidemia (13.5%). With an average body mass index of 23.10 kg/m² (SD = 5.77), 94 (50.9%) of patients were abnormal scales, which were underweight (16.8%) and overweight (34.1%) (Table 2).

Depressive symptoms and socio-demographic or clinical characteristics of the participants

The findings showed that 43.2% of the participants had depressive symptoms. They were severe depressive symptoms 2.2%, moderate depressive symptoms 5.9%, and mild depressive symptoms 35.1%. The PHQ-9 scores were between 0 and 23 points, with an average of 7.77 points (SD = 4.79) (Figure 2).

Among the socio-demographic characteristics, sex, age, religion, education, occupation, right to access healthcare, family characteristics, family members, and monthly household income were not associated with depressive symptoms in patients with SLE. Household income sufficiency was significantly associated with depressive symptoms in patients with SLE ($p = 0.008$), and patients with different marital statuses tended to be associated with depressive symptoms ($p = 0.051$) (Table 1).

Among the clinical characteristics, duration of disease was not associated with depressive symptoms in patients with SLE. Prednisolone dosage ($p = 0.004$), disease flares especially both in kidney system ($p = 0.007$) and muscles ($p = 0.044$), and body mass index ($p = 0.008$) were significantly associated with

depressive symptoms in patients with SLE and patients with complication of avascular necrosis tended to be associated with depressive symptoms ($p = 0.061$) (Table 2).

Univariable logistic regression statistical analysis of depressive symptoms of the participants

Patients with disease flare ($p = 0.002$), organ damage ($p = 0.036$), moderate or severe pain ($p = 0.044$) ($p = 0.002$), fatigue ($p = 0.000$), taking prednisolone ≥ 15 mg daily ($p = 0.004$), moderate or low satisfied of body image ($p = 0.008$) ($p = 0.000$), moderate or low social support ($p = 0.001$) ($p = 0.002$), and leftover of income ($p = 0.009$) significantly associated with depressive symptoms in patients with SLE (Table 3).

Multivariable logistic regression statistical analysis of depressive symptoms of the participants

Patients with severe pain ($p = 0.026$), fatigue ($p = 0.031$), taking prednisolone ≥ 15 mg daily ($p = 0.004$), low satisfied of body image ($p = 0.004$), and moderate or low social support ($p = 0.013$) ($p = 0.009$) significantly associated with depressive symptoms in patients with SLE. Patients with taking prednisolone 6 to 14 mg daily ($p = 0.091$) tended to be associated with depressive symptoms (Table 3).

Table 1
Personal characteristics of the participants with or without depressive symptoms
(n=185)

	Depress		Non-depress	
	Total (%)	N (%)	N (%)	p-value
Sex				
Female	178 (96.2)	79 (44.4)	99 (55.6)	0.142‡
Male	7 (3.8)	1 (14.3)	6 (85.7)	
Age (year)				
18 - 35	55 (29.7)	24 (43.6)	31 (56.4)	0.944...
36 - 59	130 (70.3)	56 (43.1)	74 (56.9)	
(Min = 19, Max = 59, Mean = 42.16, SD = 10.78)				
Marital status				
Single	97 (52.4)	46 (47.4)	51 (52.6)	0.051‡
Married	69 (37.3)	22 (31.9)	47 (68.1)	
Divorce	12 (6.5)	8 (66.7)	4 (33.3)	
Widowed	7 (3.8)	4 (57.1)	3 (42.9)	
Religion				
Buddhism	177 (95.7)	75 (42.4)	102 (57.6)	0.157‡
Christianity	4 (2.2)	2 (50)	2 (50)	
Islam	3 (1.6)	3 (100)	0 (0)	
Hindu	1 (.5)	0 (0)	1 (100)	
Education				
No formal education	5 (2.7)	3 (60)	2 (40)	0.553...
Primary	20 (10.8)	11 (55)	9 (45)	
Secondary	65 (35.1)	30 (46.2)	35 (53.8)	
Bachelor	79 (42.7)	30 (38)	49 (62)	
Post-graduate	16 (8.6)	6 (37.5)	10 (62.5)	
Occupation				

		Depress	Non-depress	
Unemployment	52 (28.1)	27 (51.9)	25 (48.1)	0.645...
Civil servant	36 (19.5)	13 (36.1)	23 (63.9)	
Employee	35 (18.9)	15 (42.9)	20 (57.1)	
Self-employed	34 (18.4)	12 (35.3)	22 (64.7)	
Labor	24 (13.0)	11 (45.8)	13 (54.2)	
Agriculturist	4 (2.2)	2 (50)	2 (50)	
Right to access healthcare				
Social security scheme	72 (38.9)	28 (38.9)	44 (61.1)	0.509...
Universal scheme	68 (36.8)	33 (48.5)	35 (51.5)	
Cash or insurance	45 (24.3)	19 (42.2)	26 (57.8)	
Family				
Single	150 (81.1)	66 (44)	84 (56)	0.667‡
Extend	35 (18.9)	14 (40)	21 (60)	
Family members (persons)				
1 - 3	107 (57.8)	51 (47.7)	56 (52.3)	0.166...
4 - 5	60 (32.4)	20 (33.3)	40 (66.7)	
> 5	18 (9.7)	9 (50)	9 (50)	
(Min = 1, Max = 11, Mean = 3.54, SD = 1.72)				
Household monthly income (baht)				
< 10,000	5 (2.7)	4 (80)	1 (20)	0.262...
10,000 - 25,000	63 (34.1)	31 (49.2)	32 (50.8)	
25,001 - 40,000	38 (20.5)	16 (42.1)	22 (57.9)	
40,001 - 60,000	46 (24.9)	17 (37.0)	29 (63.0)	
> 60,000	33 (17.8)	12 (36.4)	21 (63.6)	
(Min = 3,000, Max = 200,000, Mean = 45,262.76, SD = 35,516.22)				
Household income sufficiency				
Leftover	90 (48.6)	30 (33.3)	60 (66.7)	0.008...

		Depress	Non-depress
No leftover	95 (51.4)	50 (52.6)	45 (47.4)
... the p-value associated with Chi-square test, ‡ p-value from Fisher's Exact test			

Table 2
Clinical characteristics of the participants with or without depressive symptoms
(n=185)

		Depress	Non-depress	
	Total	N (%)	N (%)	p-value
Duration of disease (year)				
≤ 5	39 (21.1)	17 (43.6)	22 (56.4)	0.847...
6 - 10	51 (27.6)	20 (39.2)	31 (60.8)	
11 - 20	68 (36.8)	32 (47.1)	36 (52.9)	
> 20	27 (14.6)	11 (40.7)	16 (59.3)	
(Min = 0.50, Max = 38, Mean = 12.84, SD = 8.09)				
Prednisolone (mg/day)				
Unused	51 (27.6)	18 (35.3)	33 (64.7)	0.004...
1 - 5	89 (48.1)	32 (36)	57 (64)	
6 - 14	13 (7)	8 (61.5)	5 (38.5)	
≥ 15	32 (17.3)	22 (68.8)	10 (31.2)	
(Min = 0, Max = 40, Mean = 5.90, SD = 7.71)				
Disease flares				
Non-disease flare	145 (78.4)	54 (37.2)	91 (62.8)	0.005...
Disease flare	40 (21.6)	26 (65)	14 (35)	
Disease flares in body systems (≥ 1 answer)				
Kidney system	16 (8.6)	12 (75)	4 (25)	0.007...
Muscle and joints	7 (3.8)	6 (85.7)	1 (14.3)	0.044‡
Hematology	7 (3.8)	5 (71.4)	2 (28.6)	0.242‡
Skin	11 (5.9)	5 (45.5)	6 (54.5)	1.000‡
Other congenital diseases				
Nom-congenital disease	24 (13)	8 (33.3)	16 (66.7)	0.294...
Have congenital disease	161 (87)	72 (44.7)	89 (55.3)	
Congenital disease (≥ 1 answer)				

		Depress	Non-depress	
Lupus nephritis	87 (47)	36 (37.6)	51 (49.4)	0.630...
Hypertension	36 (19.5)	16 (44.4)	20 (55.6)	0.871...
Dyslipidemia	25 (13.5)	10 (40)	15 (60)	0.725...
Anemia	18 (97)	9 (50)	9 (50)	0.543...
Diabetes	15 (8.1)	8 (53.3)	7 (46.7)	0.411...
Avascular necrosis	15 (8.1)	3 (20)	12 (80)	0.061...
Discoid	13 (7)	8 (61.5)	5 (38.5)	0.167...
Osteoporosis	12 (6.5)	7 (58.3)	5 (41.7)	0.275...
Premature menopause	12 (6.5)	4 (33.3)	8 (66.7)	0.474...
Rheumatoid arthritis	10 (5.4)	5 (50)	5 (50)	0.748‡
Chronic kidney disease	9 (4.9)	6 (66.7)	3 (33.3)	0.178‡
Body Mass Index				
Normal	91 (49.2)	29 (31.9)	62 (68.1)	0.008...
Underweight	31 (16.8)	16 (51.6)	15 (48.4)	
Overweight	63 (34.1)	35 (55.6)	28 (44.4)	
(Min = 14.52, Max = 60.40, Mean = 23.10, SD = 5.77)				
... the p-value associated with Chi-square test, ‡ p-value from Fisher's Exact test				

Table 3

Univariable & Multivariable logistic regression analysis for depressive symptoms of the participants (n = 185)

Variables (N)	Univariable			Multivariable		
	cOR	95%CI	p-value	aOR	95%CI	p-value
Biology factors:						
Disease flare (SLEDAI)						
Non-disease flare (145)	1					
Disease flare (40)	3.13	1.51, 6.51	0.002**	1.59	.30, 8.32	0.585
(Min = 0, Max = 12, Mean = 1.96, SD = 3.03)						
Organ damage (SLICC Damage Index)						
Non-organ damage (95)	1					
Organ damage (90)	1.88	1.04, 3.38	0.036*	1.33	.60, 2.93	0.478
(Min = 0, Max = 5, Mean = 0.75, SD = 0.96)						
Pain (NRS)	1	.25, 1.91	0.476	.61	.18, 2.07	0.425
Non-pain (108)	.69	1.02, 4.51	0.044*	1.53	.60, 3.91	0.379
Mild pain (22)	2.15	3.51, 217.32	0.002**	12.11	1.35, 108.46	0.026*
Moderate pain (39)	27.63					
Severe pain (16)						
(Min = 0, Max = 9, Mean = 1.95, SD = 2.63)						
Fatigue (FSS)	1	2.43, 8.45	0.000***	2.36	1.08, 5.14	0.031*
Non-fatigue (98)	4.53					
Fatigue (87)						
(Min = 1, Max = 7, Mean = 3.63, SD = 1.54)						
Prednisolone (mg/day)	1	.50, 2.11	0.937	.98	.39, 2.48	0.979
0 (51)	1.03	.84, 10.30	0.093	3.68	.81, 16.67	0.091
1-5 (89)	2.93	1.57, 10.35	0.004**	5.75	1.76, 18.80	0.004**
6-14 (13)	4.03					
≥ 15 (32)						
(Min = 0, Max = 40, Mean = 5.90, SD = 7.71)						

Variables (N)	Univariable			Multivariable		
	cOR	95%CI	p-value	aOR	95%CI	p-value
Psychology factor:						
Body image (BIS)						
High satisfied (120)	1					
Moderate satisfied (46)	2.57	1.28, 5.15	0.008**	1.86	.77, 4.46	0.163
Low satisfied (19)	18.34	4.03, 83.43	0.000***	12.49	2.23, 69.80	0.004**
(Min = 0, Max = 20, Mean = 18.39, SD = 7.18)						
Social factors:						
Social support (ESSI)						
High social support (115)	1					
Moderate social support (57)	3.14	1.63, 6.08	0.001**	2.98	1.32, 6.74	0.013*
Low social support (13)	27.43	3.43, 219.18	0.002**	17.96	1.86, 173.77	0.009**
(Min = 9, Max = 30, Mean = 22.16, SD = 6.10)						
Household income sufficiency						
Leftover (90)	1					
No leftover (95)	2.22	1.23, 4.03	0.009**	1.63	.74, 3.56	0.225
* p-value < 0.05, ** p-value < 0.01, *** p-value < 0.001						
Abbreviations: SLEDAI: the Systemic Lupus Erythematosus Activity Index, SLICC Damage Index: the Systemic Lupus International Collaborating Clinics Damage Index, NRS: Numeric Rating Scale, FSS: Fatigue Severity Scale, BIS: Body Image Scale, ESSI: the ENRICH Social Support Instrument, COR: Crude odds ratio, AOR: Adjusted odds ratio, 95% CI: 95% confidence interval.						

Discussion

A decade ago, depressive symptoms had been considered a significant mental health problem for the whole population that was nevertheless under-recognized (44), especially in chronic physical patients. In the current study, the proportion of the participants with depressive symptoms was 43.2%, consistent with prior studies (2, 3, 4, 6, 7). In contrast, 8.1% of patients faced moderate to severe depressive symptoms and could be diagnosed with depression, higher than the general Thai population (45). According to the results of our study, the biopsychosocial factors have more influence on depressive symptom severity in patients with SLE.

The association between depressive symptoms and clinical symptoms was quite different in various studies. Biology factors like disease flare, organ damage, pain, fatigue, and cumulative corticosteroid dosage were all involved (2, 21, 46). In our study, we found that depressive symptoms were in positive correlation with all those factors. However, the multivariable analysis findings did not show association with either disease flare or organ damage with depressive symptoms. Like previous studies, associations between depressive symptoms and disease flare are inconsistent because of methodological differences in measuring disease activity of SLE. Using an objective disease activity measure such as SLEDIA, there was no association between depressive symptoms (47, 48, 49, 50). Simultaneously, previous studies have suggested that patients and those with disease activity, including laboratory changes or disease damage, are more likely to have increased severity of depression in patients with SLE (3, 21). Further research with larger sample size and well-controlled assessment and study methodology may clarify and confirm these phenomena.

On the other hand, the observation in the multivariable analysis showed extreme pain, severe fatigue, and high dosage of steroid use were strongly interwoven in physical and psychiatric disorders among patients with SLE (19, 21, 30). Considering those factors and depressive symptoms altogether share norepinephrine or serotonin neurotransmitter pathway pathology in the central nervous system that can provoke visible and invisible manifestations of physiological illness. Fatigue has previously been correlated with an increased risk for depression among these patients (19), and this study strengthens these associations. Heightened pain was associated with increased depressive symptoms in this study. This evidence confirms findings in various studies demonstrating that increased pain is related to a greater risk of depressive symptoms in patients with SLE (51, 52). Depressive symptoms can also be caused by corticosteroid treatment through downregulation of brain-derived neurotrophic factors (53, 54). In our study, patients who continued taking ≥ 15 mg prednisolone daily had significant depressive symptoms comparable to mean doses of prednisolone in a previous study, 18.28 mg for patients with major depressive disorder (MDD) and 15 mg daily for patients with non-major depressive disorder (21).

Increased body mass index scores in patients were correlated with depressive symptoms (53, 54). The patients with depressive symptoms demonstrate higher levels of unemployment. Those findings could be confounding factors in depression. It likely also indicated the risk of depressive symptoms, which causes disease manifestations, disability, and productivity (19).

Dissatisfaction with one's appearance is a real problem that patients with SLE frequently face (57, 58). However, an understanding of SLE patients' feelings about their body image has been lacking in Thai research. This omission makes it difficult to evaluate the degree of body image dissatisfaction, with much of the research on body image only emphasizing patients with breast cancer (59). This gap needs to be addressed through focused research on these specific issues. From the previous studies, self-perceived appearance mediated the relationship between physical health-related quality of life and depression among patients with SLE (60, 61). Our findings corroborated previous studies. In the present study, we found that low body-image satisfaction was an enormously significant predictor of depressive

symptoms in patients with SLE, both in the univariable and multivariable analysis. Thus, a method that targets the body image and the health outcomes of patients with SLE could be effective.

Among social factors, the findings from the multivariable analysis did not show household income sufficiency was significantly associated with depressive symptoms in patients with SLE. A consistent previous examination found poverty was a significant predictor in the bivariate analysis, but not the multivariate (62). However, social support is a crucial resource for patients with SLE with a high disease burden (63). Many studies have noted the importance of social support regarding depression (64, 65, 66). Good social support has been shown to protect from depression and elevate an individual's emotional state (53). It has also been established that those depressive characteristics are associated with decreased peer-related social support (64). The univariable and multivariable analysis results found that social support was significantly associated with depressive symptoms in patients with SLE. It is clarified that social support is vital for mental health and that a decrease in relationship satisfaction is an indicator of depressive symptoms.

Strengths And Limitations

The strengths of this study include the use of the psychological instruments, which were acceptable reliability and validity in Thai populations. Moreover, independent variables were defined based on Engle's biopsychological model. It is a practical way of understanding how patients suffer physical and mental illnesses from sociology to molecular biology (67). However, this present study has several limitations. Participants were selected using inclusion/exclusion criteria, and the study was performed at a single medical center. Therefore, it may not represent patients with several backgrounds. Additionally, the role of inflammation and genetic susceptibility for the emergence of depressive symptoms was not assessed. Thus, more psychoanalytic research is needed to clarify the relationship between the immune system of disease activity and a patient's psychological function.

Conclusion

In summary, depressive symptoms are highly prevalent among Thai patients with SLE. Depressive symptoms in those patients come from various causes is particularly the perceiving of individual patients. Treatments of depressive symptoms may benefit patients with extreme pain, fatigue, high prednisolone dosage, low satisfaction of body image, and low social support. Further study of biopsychosocial factors is necessary to fully comprehend the causes and potential management for debilitating depression in patients with SLE.

Abbreviations

SLE: Systemic Lupus Erythematosus; PHQ-9: the Patient Health Questionnaire-9; BPS: the Biopsychosocial Model; SLEDAI: the Systemic Lupus Erythematosus Activity Index; SLICC Damage Index: the Systemic Lupus International Collaborating Clinics Damage Index; NRS: Numeric Rating Scale; FSS:

Fatigue Severity Scale; BIS: Body Image Scale; ESSI: the ENRICH Social Support Instrument; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; NSO: the National Statistical Office of Thailand; ICD-10: International Classification of Diseases 10th Revision; COVID-19: Coronavirus Disease of 2019; ACR: the Revised American College of Rheumatology Classification; SPSS: Statistical Package for the Social Sciences; MDD: Major Depressive Disorder

Declarations

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Authors' contributions

All authors made substantial contributions to the study concept and design and acquisition of data. NN¹ did the initial analysis, interpretation of data and drafted the initial manuscript. AS² provided feedback on the initial investigation. NN¹, AS², WP² were involved in developing and revising the manuscript. All authors read and approved the final manuscript before submission.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethical approval of this study was granted by the Institutional Review Board Faculty of Nursing, Mahidol University (IRB-NS2020/42.3010), and the Institutional Review Board Faculty of Medicine, Chulalongkorn University, Thailand (IRB No. 099/64). Written informed consent was obtained from all study participants before enrollment. All procedures were performed in accordance with the Declaration of Helsinki, The Belmont Report, CIOMS guideline and International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

Biopsychosocial factors of depressive symptoms in patients with SLE

Figure 2

Prevalence of depressive symptoms in patients with SLE