Factors Associated with Psychosomatic Disorders Among Systemic Lupus Erythematosus (SLE) Patients During the Coronavirus Disease 2019 (COVID-19) Pandemic

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ABSTRACT

Background: *The COVID-19 pandemic has affected physical and mental health. SLE patients are prone to psychosomatic disorders which can decrease their quality of life. This study aimed to determine the factors associated with psychosomatic disorders among SLE patients during the COVID-19 pandemic.* ***Methods:*** *This was a cross-sectional study of adult female SLE patients from the outpatient clinic of Cipto Mangunkusumo Hospital, Jakarta. Data regarding psychosomatic disorders were collected using SCL-90 questionnaires, and data on demographic factors, perception of COVID-19 conditions, perception of stress, psychosocial stressors, disease activity (MEX-SLEDAI), and treatment were also collected. Bivariate analysis for categorical data was conducted using the Chi square test. Variables with a p-value <0.25 were further analyzed with logistic regression, and p-values <0.05 were considered significant. Meanwhile, data per domain were analyzed using the Mann-Whitney test with p-values < 0.05 being considered significant.* ***Results:*** *There were 200 female SLE patients recruited. More than half of the subjects (54%) experienced psychosomatic disorders. From multivariate analysis, high educational level, moderate and high psychosocial stressors, and very severe disease activity level were found to be significantly associated with the occurrence of psychosomatic disorders in SLE patients during the COVID-19 pandemic.* ***Conclusion:*** *Education level, psychosocial stressors, and disease activity*

level were found to be significantly associated with the occurrence of psychosomatic disorders in SLE patients during the COVID-19 pandemic.

Keyword: *psychosomatic, lupus, COVID 19.*

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) was a global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV 2) that first emerged in Wuhan in December 2019.[1] It rapidly spread to various parts of the world and was declared a pandemic by the World Health Organization (WHO) in January 2020. COVID-19 continues to be a concern for patients with special conditions, such as geriatric patients and patients with comorbidities (diabetes mellitus, cardiovascular diseases, chronic lung diseases, or autoimmune patients).[2,3] Autoimmune diseases are associated with a higher risk of severe COVID-19 outcomes.[4] According to research by Sawalha AH et al., severe COVID-19 cases were found in patients with systemic lupus erythematosus (SLE).[5] This is linked to inherent immune dysfunction and immunosuppression due to autoimmune treatments.[4]

The COVID-19 pandemic has affected SLE patients, not only physically but also mentally.[6] Common disturbances experienced by SLE patients include emotional disturbances (feeling sad, symptoms of depression, anxiety symptoms, fear, anger), sleep disturbances, fatigue, and pain. These various disruptions decrease quality of life for SLE patients.[7] The number of psychosomatic disturbances during three different COVID-19 waves were increasing.[8] Study by Wankowicz et al revealed that during COVID-19 pandemic, SLE patients experienced more anxiety, depression, and sleep disorder compared to healthy control.[9]

Some factors can affect psychosomatic disorders. Psychosomatic disorders may be found more often among older adults.[10] This age group has more risk of contracting COVID-19 and developing severe disease which can cause more fear among older adults.[11] Level of stress can also affect psychosomatic disorder. The higher the level of stress, the higher the risk of physical and mental health problem.[12] Level of stress depends on the perception of stress. Same level of stress can cause different effect on different individual.[13] SLE disease activity may also affect psychosomatic disorder. Lower disease activity can decrease psychosomatic disorder.[14-15] History of COVID-19 infection might also affect psychosomatic disorder by causing stigma which could lead to fear of isolation and discrimination.[16] Corticosteroid treatment can also contribute to psychosomatic disorder directly by its psychiatric adverse effects.[17]

There is no published study about psychosomatic disorders among SLE patients during COVID-19 pandemic in Indonesia. To anticipate and prevent psychosomatic disorders among SLE patients during COVID-19 pandemic or other pandemic in the future, it is important to know factors associated with these disorders so that quality of life of SLE patients can be improved. This study aimed to determine whether age, education level, perception of COVID-19, perception of stress, psychosocial stressors, SLE disease activity, corticosteroid, and history of COVID-19 infection were associated with psychosomatic disorders among SLE patients during the COVID-19 pandemic.

METHODS

Study Design and Participants

We conducted a cross-sectional study that recruited SLE patients from the outpatient clinic of Cipto Mangunkusumo Hospital, Jakarta Indonesia, from September to October 2021. The inclusion criteria were female SLE patients with ages of 18 years or older. SLE patients who refused to participate were excluded.

Ethics

We obtained ethical approval with number: KET-37/UN2.F1/etik/PPM.00.02/2021 from The Research Ethics Committee of the Faculty

of Medicine, Universitas Indonesia. The participation was on voluntary base and all participants provided their written informed consent.

Study Procedures

Participants were recruited using consecutive sampling method. SLE patients who met study criteria were offered to participate in this study. After giving written informed consent, the participants were interviewed and examined to get demographical data (age, education level, marital status) and clinical data (history of COVID-19, family history of COVID-19, SLE organ involvement, SLE disease activity, and medications). Participants were also interviewed to evaluate perceptions of COVID-19, stress perception, psychosocial stressors, and psychosomatic disorders.

Outcome Measures

Data regarding perceptions of COVID-19, stress perception, psychosocial stressors, and psychosomatic disorders were obtained using validated questionnaires: questionnaires from a study by Widhani A et al.,[18] Perceived Stress Scale,[19,20] Holmes and Rahe Stress Scale,[21] and SCL-90, respectively.[22] Patients perceptions on the effect COVID-19 pandemic to their health condition were classified as anxious and disturbing activities; worried, but not disturbing activities; and not worried.[18] Perceived Stress Scale (PSS) classified patients stress perception in to mild (score 0-13), moderate (score 14-26), and severe (score 27-40) stress.[12,19] Holmes and Rahe Stress Scale assessed various stressors from family, environment, job, and education that can affect physical and mental health. This scale classified patients as low (score <150), moderate (score 150-299), and high risk (score >300).[20]

SCL-90 consists of ninety questions about psychological problems and symptoms distress. This uses a self-reporting measurement in which participants answer on a five-point Likert scale ranging from 0 (none) to 4 (extreme). SCL-90 reports nine symptom dimensions for the past 1 month: somatization, obsessive-compulsive disorder, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism.[22] Score higher than 60 from SCL-90 indicate that the respondent has a psychosomatic disorder.[23]

Data on SLE disease activity level were assessed using the Mexican version of the Systemic Lupus Erythematosus Disease Activity Index (MEX-SLEDAI) score. Corticosteroid dose was classified into <7.5–30 mg/day; 7.5–30 mg/day and >30 mg/day equivalent to prednisone.

Statistical Analysis

Analysis was conducted to examine the relationships between demographic factors (age and education level), perception of COVID-19 conditions, perception of stress, psychosocial stressors, and clinical factors (disease activity level, corticosteroid therapy, and history of COVID-19 infection) with psychosomatic disorders among SLE patients during the COVID-19 pandemic. All data were processed using Stata. Bivariate analysis for categorical data was conducted using the Chi square test. Variables with a p-value <0.25 were further analyzed with logistic regression, and p-values <0.05 were considered significant. Meanwhile data per domain were analyzed using the Mann-Whitney test with p-values <0.05 being considered significant.

RESULTS

This study involved 200 female SLE patients who met the study criteria. Characteristics of the demographic and clinical data of the subjects can be seen in **Table 1.** The median age was 32 (IQR 25; 39) years old. The majority of the subjects were 18-39 years old (75.5%), married (54%), and had a low education level (57.5%). More than half the subjects had nephritis lupus (51.5%). All subjects were receiving corticosteroids for SLE treatment and most of them were also receiving hydroxychloroquine (70%). About 79.5% of SLE patients expressed concern about the pandemic but reported that it did not interfere with their daily activities. Only 9% of patients reported that their activities were disrupted.

More than half of the subjects (54%) experienced psychosomatic disorders. The median (IQR) scores for each domain of psychosomatic disorders were 10

Table 1. Characteristics of Demographic and Clinical Data of Study Subjects (n=200).

Variable	n (%)
Age, n (%)	
>60 years	1 (0.50)
40-59 years	48 (24.0)
18-39 years	151 (75.50)
Marital Status	
Married	108 (54.0)
Divorced	7 (3.50)
Unmarried	85 (42.50)
Education Level, n (%)	
No schooling	3 (1.50)
Elementary school	14 (7.0)
Junior high school	98 (49.0)
High school	31 (15.50)
Diploma/bachelor degree	54 (27.0)
SLE organ involvement	
Neuropsychiatric	15(7.5)
Renal	103(51.5)
Hematological	86(43.0)
Musculoskeletal	187(93.5)
Mucocutaneus	178(89.0)
Other	11(5.5)
Medications	
Corticosteroid	200(100.0)
Hydroxychloroquine	140(70.0)
Mycophenolate sodium	112(56.0)
Azathioprine	30(15.0)
Cyclosporine	7(3.5)
Cyclophosphamide	0(0.0)
Perception of COVID-19 Conditions	
Anxious and disturbing activities	18 (9.0)
Worried but not disturbing	159 (79.50)
Not worried	12 (11.50)
Perception of Stress	
Severe stress (score 27-40)	11 (5.5)
Moderate stress (score 14-26)	169 (84.5)
Mild stress (score 27-40)	20 (10.0)
Psychosocial Stressors	
High risk (score >300)	24 (12.0)
Moderate risk (score 150-299)	36 (18.0)
Low risk (score <150)	140 (70.0)
Disease Activity Level (MEX SLEDAI), n (%)	
Very severe (≥14)	59 (29.5)
Severe (10-13)	27 (13.5)
Moderate (6-9)	51 (25.5)
Mild (2-5)	45 (22.5)
Remission (0-1)	18 (9.0)
Corticosteroid Therapy	
>30 mg/day equivalent to prednisone	43 (21.50)
7.5 – 30 mg/day equivalent to prednisone	90 (45.00)
<7.5 – 30 mg/day equivalent to prednisone	67 (33.50)
History of COVID-19	
Yes	41 (20.5)
No	159 (79.5)
Family History of COVID-19	
Yes	80 (40.0)
No	120 (60.0)
Psychosomatic Disorders	
Yes	108 (54.0)
No	92 (46.0)

(4; 18) for somatization, 9 (4; 17) for obsessive-compulsive disorder, 7 (2; 13) for interpersonal sensitivity, 10 (4-16) for depression, 4 (1-10) for anxiety, 4 (1-6) for hostility, 3 (1-7) for phobic anxiety, 3 (1-7) for paranoid ideation, and 4 (1-7) for psychoticism. The median score for each domain of psychosomatic disorders based on the independent variables can be seen in **Table 2**. Disease activity was significantly related to all domains in psychosomatic disorder, except for anxiety, depression, and obsessive-compulsive disorder. History of COVID 19 infection was related to hostility and others, while perception of COVID 19 conditions was related to the phobic anxiety domain.

Bivariate tests were conducted to assess the relationship between demographic factors (age, education level), perception of COVID-19 conditions, perception of stress, psychosocial stressors, and clinical factors (disease activity level, corticosteroid therapy, and history of COVID-19 infection) with psychosomatic disorders in SLE patients during the COVID-19 pandemic. Bivariate analysis (**Table 4**) indicated a significant relationship between moderate psychosocial stressors and very severe disease activity level with the occurrence of psychosomatic disorders, with p-values of <0.0001 and 0.011, respectively. The variables with p-values <0.25, namely education level, psychosocial stressors, disease activity, and corticosteroid dose, were further subjected to multivariate analysis. From multivariate analysis, high education level, moderate and high psychosocial stressors, and very severe disease activity level were found to be significantly associated with the occurrence of psychosomatic disorders in SLE patients during the COVID-19 pandemic.

DISCUSSION

SLE is a chronic autoimmune disease that can involve more than one organ and is commonly found in women of reproductive age.[24,25] Most of our subjects were among the age group of 18-39 years (75.5%). Research by

Table 2. Scores for each domain in SCL-90

Variables	Domain SCL-90									
	Somatization	p-value	Obsessive-compulsive disorder	p-value	Interpersonal sensitivity	p-value	Depression	p-value	Anxiety	p-value
Age		0.890		0.087		0.208		0.135		0.300
>= 40 years	12 (5-18.5)		9 (4.5-16.5)		5 (0.5-17)		7 (1.5-17)		3 (0.5-9)	
< 40 years	10 (4-17)		9 (4-18)		8 (3-13)		11 (5-16)		4 (1-10)	
Education Level, n (%)		0.312		0.160		0.862		0.490		0.590
High (diploma/ bachelor)	10.5 (5-16.25)		12.5 (5.75-18.25)		8 (3-12.25)		11 (5.75-15.25)		4 (2-9.25)	
Middle (senior high school)	8 (1-20)		7 (3-17)		5 (2-14)		10 (2-16)		3 (0-9)	
Low (junior high school or lower)	10 (4-19)		9 (4-16)		6 (2-12)		9 (3-18)		4 (1-10)	
Perception of COVID-19 Conditions, n (%)		0.154		0.084		0.051		0.053		0.165
Anxious, disturbing activities	14.5 (6.75-21.25)		16 (7.75-21.25)		12.5 (4-19.5)		14.5 (8.75-21)		10 (2-13.75)	
Worried, not disturbing	10 (4-17)		9 (3-16)		6 92-12)		10 (3-16)		4 (1-9)	
Not worried	9 (5-20)		9 (6-14)		7 (3-11)		7 (3-14)		3 (2-7)	
Perception of Stress, n (%)		0.844		0.707		0.572		0.487		0.523
Severe stress	6 (1-23)		10 (8-35)		9 (4-26)		14 (3-17)		4 (2-23)	
Moderate stress	11 (4-17)		9 (4-16.5)		7 (2-12)		10 (4-16)		4 (1-9)	
Mild stress	9 (4-19,5)		8 (2-18)		6.5 (0-13)		11.5 (3.25-17)		3.5 (1.2 5-10.75)	
Psychosocial Stressor, n (%)		0.619		0.290		0.525		0.509		0.519
High risk	11.5 (6-15.5)		11.5 (7-18.75)		9.5 (4-15.25)		10.5 (6.5-15.75)		6 (2-9)	
Moderate risk	12 (5.25-17)		10.5 (4.25-16.75)		7.5 (2.25-13)		10.5 (4.5-16)		5.5 (1.25-9.75)	
Low risk	9 (4-19.75)		9 (3-17.75)		6 (2-12.75)		9.5 (2-16.75)		3 (1-10)	
Disease Activity Level, n (%)		<0.0001*		0.071		0.022*		0.018*		0.035*
Very severe	14 (9-24)		11 (6-21)		10 (5-16)		10 (5-16)		6 (2-13)	
Severe	12 (8-16)		9 (5-17)		6 (2-12)		6 (2-12)		4 (2-8)	
Moderate	6 (2-16)		9 (2-15)		5 (2-12)		8 (3-14)		4 (1-9)	
Mild	7 (3-13.5)		7 (3-14.5)		5 (1-12.5)		6 (1.5-14.5)		2 (1-7.5)	
Remission	8.5 (1.75-20.25)		12.5 (7.25-18.5)		8.5 (5-13.5)		15 (4.75-25.25)		9 (0-14.25)	
Corticosteroid Therapy, n (%)		0.909		0.821		0.806		0.913		0.931
>30 mg/day equivalent to prednisone	11 (4-21)		9 (4-19)		8 (2-13)		11 (2-18)		4 (1-10)	
7.5 – 30 mg/day equivalent to prednisone	10 (4-19.25)		9 (4-15.25)		6.5 (3-13)		10 (4-16)		4 (1-10)	
<7.5 – 30 mg/ day equivalent to prednisone	10 (4-16)		9 (4-18)		6 (2-13)		10 (4-17)		3 (1-10)	
History of COVID-19, n (%)		0.178		0.117		0.085		0.101		0.196
Yes	12 (5-22)		11 (6.5-20)		8 (5-15.5)		11 (5.5-20)		6 (1.5-10.5)	
No	10 (4-17)		9 (3-16)		6 (2-13)		10 (3-16)		4 (1-9)	
Family History of COVID-19, n (%)		0.320		0.229		0.293		0.388		0.164
Yes	11.5 (5-20)		10 (5.25-18.75)		8.5 (2.5-15)		11 (4-16)		5 (2-10)	
No	9.5 (4-17)		9 (4-16)		6.5 (2-11.75)		9.5 (3.25-16)		3 (1-10)	

All data in median (IQR), * p<0.05

Table 3. Scores for each domain in SCL-90 (continued)

Variables	Domain SCL-90									
	Hostility	p-value	Phobic anxiety	p-value	Paranoid ideation	p-value	Psychoticism	p-value	Others	p-value
Age		0.391		0.785		0.780		0.339		0.513
>= 40 years	3 (0-7)		3 (1-7)		2 (0-7.5)		3 (0-10)		7 (2 -9.5)	
< 40 years	4 (1-6)		3 (1-7)		3 (1-6)		4 (1-9)		7 (4-10)	
Education Level, n (%)		0.418		0.302		0.423		0.723		0.971
High (diploma/ bachelor)	4 (2-8)		3.5 (1-7.5)		3 (1-7)		4 (1.75-10.25)		7 (4-9)	
Middle (senior high school)	3 (1-6)		2 (0-6)		2 (0-9)		5 (0-11)		6 (3-12)	
Low (junior high school or lower)	4 (1-6)		3 (1-7)		3 (0-6)		3 (0-9)		6 (3-10)	
Perception of COVID-19 Conditions, n (%)		0.074		0.039*		0.13		0.127		0.136
Anxious, disturbing activities	5 (2.75-10.75)		5 (3-11)		4.5 (2.75-9.5)		6.5 (1-18)		8 (5.75-11.25)	
Worried, not disturbing	3 (1-6)		3 (1-7)		3 (0-6)		4 (0-9)		7 (3-10)	
Not worried	3 (2-5)		3 (2-6)		3 (1-6)		2 (1-6)		5 (2-8)	
Perception of Stress, n (%)		0.190		0.721		0.642		0.932		0.358
Severe stress	5 (3-11)		4 (0-12)		2 (1-13)		2 (0-23)		9 (3-14)	
Moderate stress	3 (1-6)		3 (1-7)		3 (1-6)		4 (1-9)		7 (4-10)	
Mild stress	3.5 (1.25-8)		3 (1-5.5)		3 (0-9.75)		3.5 (0.25-10)		5.5 (2-8)	
Psychosocial Stressor, n (%)		0.295		0.224		0.630		0.479		0.198
High risk	5 (3-6.75)		5 (3-6.75)		4 (1-7.5)		4.5 (2-10.75)		7 (6-10)	
Moderate risk	3.5 (1-6.75)		3.5 (1-6.75)		3 (1-6)		4 (0-9)		7 (4-10.75)	
Low risk	3 (1-6)		3 (1-6)		3 (0-7)		4 (0-9)		6 (3-9)	
Disease Activity Level, n (%)		0.006*		0.015*		0.129		0.050		0.007*
Very severe	5 (2-7)		4 (2-10)		4 (1-0)		6 (2-13)		8 (5-12)	
Severe	2 (1-5)		4 (1-6)		3 (1-6)		3 (1-7)		7 (5-11)	
Moderate	3 (1-6)		3 (0-6)		2 (0-6)		3 (0-8)		6 (2-9)	
Mild	3 (0-5)		2 (1-5)		2 (0.5-6)		2 (0-9)		5 (2.5-8)	
Remission	4.5 (2-8.25)		3.5 (0.75-8.25)		3 (0.75-6.25)		8 (1.5-11)		8.5 (3.75-11)	
Corticosteroid Therapy, n (%)		0.984		0.604		0.758		0.982		0.885
>30 mg/day equivalent to prednisone	3 (1-6)		4 (2-9)		3 (1-6)		4 (0-9)		7 (3-11)	
7.5 – 30 mg/ day equivalent to prednisone	4 (1-7)		3 (1-7)		3 (1-7)		4 (1-9)		7 (3.75-9)	
<7.5 – 30 mg/ day equivalent to prednisone	3 (1-6)		3 (1-6)		2 (1-7)		4 (0-10)		7 (3-9)	
History of COVID-19, n (%)		0.042*		0.331		0.094		0.116		0.027*
Yes	4(2-8.5)		3 (1-7)		4 (1.5-9.5)		5 (2-10)		8 (5-11)	
No	3 (1-6)		4 (1-8)		3 (0-6)		3 (0-9)		6 (3-9)	
Family History of COVID-19, n (%)		0.720		0.192		0.210		0.346		0.464
Yes	4 (1-7)		3.5 (2-8)		3.5 (1-8)		5 (1-10)		7 (3-10)	
No	3 (1-6)		3 (1-6)		2.5 (1-6)		3 (0-9)		6 (3.25-9)	

All data in median (IQR), * p<0.05

Table 4. Factors related to psychosomatic disorders among SLE patients during the COVID-19 pandemic.

Variables	Psychosomatic Disorder		PR (95%CI)	p-value	PR (95%CI)	p-value
	Yes	No				
Demographic Factors						
Age, n (%)						
>= 40 years	27 (55.10)	22 (44.90)	1.027 (0.765 – 1.377)	0.858		
< 40 years	81 (53.64)	70 (46.36)				
Education Level, n (%)						
High (diploma/bachelor)	35 (64.81)	19 (35.19)	1.242 (0.954 – 1.617)	0.107	1.229 (1.016 – 1.643)	0.036*
Middle (senior high school)	13 (41.94)	18 (58.06)	0.803 (0.512 – 1.261)	0.342		
Low (junior high school or lower)	60 (52.17)	55 (47.83)	Ref			
Perception of COVID-19 Conditions, n (%)						
Anxious and disturbing activities	11 (61.11)	7 (38.89)	1.081 (0.645 – 1.810)	0.767		
Worried but not disturbing	84 (52.83)	75 (47.17)	0.934 (0.633 – 1.378)	0.733		
Not worried	13 (56.52)	10 (43.48)	Ref			
Perception of Stress, n (%)						
Severe stress	4 (36.36)	7 (63.64)	0.661 (0.274 – 1.591)	0.356		
Moderate stress	93 (55.03)	76 (44.97)	1.000 (0.657 – 1.523)	0.998		
Mild stress	11 (55.0)	9 (45.0)	Ref			
Psychosocial Stressor, n (%)						
High risk	15 (62.50)	9 (37.50)	1.346 (0.940 – 2.926)	0.104	1.413 (1.013 – 1.970)	0.042*
Moderate risk	28 (77.78)	8 (22.22)	1.675 (1.304 – 2.150)	<0.0001*	1.496 (1.182 – 1.894)	0.001*
Low risk	65 (46.43)	75 (53.57)	Ref			
Clinical Factors						
Disease Activity Level, n (%)						
Very severe	52 (88.14)	7 (11.86)	1.983 (1.171 – 3.356)	0.011*	1.820 (1.076 – 3.078)	0.025*
Severe	11 (40.74)	16 (59.26)	0.916 (0.459 – 1.827)	0.805		
Moderate	23 (45.10)	28 (54.90)	1.014 (0.556 – 1.849)	0.962		
Mild	14 (31.11)	31 (68.89)	0.700 (0.355 – 1.377)	0.302		
Remission			Ref			
Corticosteroid Therapy, n (%)						
>30 mg/day equivalent to prednisone	28 (65.12)	15 (34.88)	1.322 (0.952 – 1.834)	0.095	1.078 (0.803 – 1.448)	0.616
7.5 – 30 mg/day equivalent to prednisone	47 (52.22)	43 (47.78)	1.060 (0.774 – 1.451)	0.715		
<7.5 – 30 mg/day equivalent to prednisone	33 (49.25)	34 (50.75)	Ref			
History of COVID-19, n (%)						
Yes	23 (56.10)	18 (43.90)	1.049 (0.771 – 1.427)	0.759		
No	85 (53.46)	74 (46.54)				
Family History of COVID-19, n (%)						
Yes	45 (56.25)	35 (43.75)	1.071 (0.827 – 1.387)	0.600		
No	63 (52.50)	57 (47.50)				

*p< 0.05

Macejova Z et al. found the highest number of SLE cases to be in the age group of 30-38 years, accounting for 32.8%.[26]

We only included female SLE patients because they constitute the majority of SLE patients. Study by Peralta-Ramirez et al showed that female SLE patients had higher scores across all dimensions of SCL-90-R which was used to assess psychosomatic disorder, except for paranoid ideation, compared to healthy females. This could be explained by the medical symptoms they experienced, disease course, pain, treatment, and the loss of function.[27]

Psychosomatic disorder is a condition caused by imbalance of hypothalamus-pituitary-adrenal axis and sympathetic nerve system. Stressful life events can affect neuroendocrine immune function. This mediated by hormones, neurotransmitters, and cytokines which then can result in the dysregulation of immune response.[28,29]

SLE patients are vulnerable to psychological problems during heath emergency situations, like the COVID-19 pandemic. Lockdown measures, fears of becoming infected, frustration, loneliness, and difficulties in gaining medical treatments during periods like this can affect psychological well-being. A study by Santos-Ruiz et al revealed that SLE patients evaluated during the lockdown period of COVID-19 had significantly higher scores in global scores and in some subdomains of SCL-90-R, namely anxiety, depression, interpersonal sensitivity, phobic anxiety, and psychoticism, compared to SLE patients evaluated before the period of COVID-19 lockdown.[30]

More than half of the subjects (54%) in our study experienced psychosomatic disorders during the COVID-19 pandemic. A study by Tian et al of Chinese citizens during COVID-19 pandemic from 31 January to 2 February 2020 using SCL-90 showed that more than 70% of participants had moderate and higher levels of psychological symptoms.[31] Psychosomatic disorders can cause decreased quality of life, loss of employment, disability, and problems in relationships. Furthermore, they can worsen psychiatric problems.[32] Psychosomatic disorders like depression can also affect adherence to medication.[33] A study published in 2018 evaluating psychosomatic disorder among SLE patients also showed higher scores across all dimensions of SCL-90-R compared to healthy controls, except for paranoid ideation.[27]

Our study found that disease activity, psychosocial stressors, and educational level were significantly associated with the occurrence of psychosomatic disorders in SLE patients during the COVID-19 pandemic, while perception of COVID-19 conditions and perception of stress were not. A study by Liao et al showed that anxiety and depression were more frequent in the moderate-severe active SLE group than in the mild active-inactive SLE group.[34] This differs to the results of our study, which used SCL-90, as disease activity was significantly related to all domains of psychosomatic disorder, except for anxiety and depression. In another study by Peralta-Ramirez et al in 2018, it was revealed that disease activity (SLEDAI score) was significantly associated with psychopathological manifestation among SLE patients which was measured using SCL-90-R. SLE patients with higher disease activity have more severe symptoms or pain and need more aggressive treatments which can affect their psychological condition. In contrast with our results, this study, which was conducted before the COVID-19 pandemic, also revealed that perceived stress (measured by the perceived stress scale) was also significantly associated with psychopathological manifestations which could be explained by the unpredictable and chronic nature of the disease perceived by SLE patients.[27] Another study among health care workers showed that perceived stress was one of the significant predictors of psychosomatic disorder during the COVID-19 pandemic.[35] Our study found that perceived stress did not have significant relation with psychosomatic disorders, while psychosocial stressors did. This is probably related to the time our study was conducted, September to October 2021, more than one year after COVID-19 had been declared a pandemic. Over time, perceived stress related to COVID-19 may resolve. A study by Egede et al of adults with positive COVID-19 tests revealed that perceived stress decreased at 3 months compared to the baseline.[36] Another study by Santos-Ruiz showed that there was no

significant difference in the level of perceived stress between SLE patients evaluated during the lockdown period of COVID-19 and SLE patients evaluated before the period of COVID-19 lockdown.[30] Psychosocial stressors still had a significant relationship with psychosomatic disorder because the Holmes and Rahe stress scale, which we used to measure psychosocial stressors, included some of the changes that could happen during the COVID-19 pandemic, including death of a spouse, illness, health change among family members, loss of employment, and change in social or school activities.

In our study, education level was also found to be significantly associated with psychosomatic disorder. High education level had a greater incidence of psychosomatic disorder than any other education level. A study by Mei et al similarly revealed that high education level (a bachelor's degree or higher) was associated with postpartum depression among older primipara.[37] Study by Wang et al on public psychological states during COVID-19 outbreak in China also showed that higher education level significantly associated with higher depression.[38] However, our results contrasted with other studies. Studies by Mohamed et al found that level of education was negatively correlated with anxiety and depression among SLE patients, but this study was not done during COVID-19 outbreak.[39] Studies by Niemeyer et al and Kondirolli et al among non-SLE populations showed that higher education was associated with lower depression and anxiety.[40,41] Education level can have an effect on mental health more than two decades later. Education can affect mental health by improving health knowledge and behavior, physical health, and women's empowerment.[41] Low education leads to fewer psychosocial resources.[40] A study by Belo et showed that retired people with a high level of education had better psychological conditions and perceptions of aging changes.[42] From our study, median scores for high education level were higher in obsessive-compulsive disorder, interpersonal sensitivity, depression, and the phobic anxiety domain although the differences were not statistically significant.

We did not find significant association between age and psychosomatic disorder. This result was similar with study by Mohamed et al which also found no association between age and mental problem among SLE patient.[39] Different study among non-SLE population showed increased in psychosomatic problem with increasing age.[10] This difference probably caused by different age group of the study population. Most SLE patients are young so that not many older adults were involved in SLE study.

We also analyzed association between corticosteroid dose and psychosomatic disorders which showed no significant association. Similar result was shown by Rafaat et al which found that corticosteroid dose was not related with major depression among SLE patients.[43] Other studies showed that corticosteroid treatment might cause increased incidence of depression or mania.[44] Study by Alturaymi et al revealed that the prevalence of mental disorder among patients using steroid was 5.5%.[45] Mechanism of how corticosteroid can cause mental disorder still unclear. One hypothesis is that corticosteroid can cause decrease in norepinephrine, corticotropin, and beta-endorphin immunoreactivity. Besides that, acute corticosteroid use can decrease left hippocampus activity, glucose metabolism in hippocampus, blood flow to posterior medial temporal lobe. Chronic corticosteroid use is associated with lower levels N-acetyl aspartate in temporal lobe and smaller volume of hippocampus. Duration of corticosteroid use is associated with atrophy of right amygdala which is a regulator of anxiety and mood.[46]

Other factors analyzed in our study were patient or family history of COVID-19 infection. We did not find significant association between these factors and psychosomatic disorder even though previous study among kidney transplant recipients revealed that patient's history of COVID-19 infection was a predictive factor of depression and anxiety during COVID 19 pandemic.[47]

Although this study was conducted during the COVID-19 pandemic and WHO has declared that the pandemic is over, the results of our study can offer valuable lessons for managing future pandemics. The high incidence of psychosomatic disorders observed could also be seen in future

pandemics. Additionally, factors identified in our study—such as education level, psychosocial stressors, and disease activity level—may also be relevant to psychosomatic disorders in non-pandemic conditions. Psychosocial stressors related to SLE might influence psychiatric symptoms because SLE is a chronic, recurring, serious, and often fatal disease. These stressors can activate the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system, while also reducing brain-derived neurotrophic factor, which can further increase anxiety and depression.[32] Higher disease activity was also related to higher anxiety and depression although in non-pandemic condition.[48]

Psychological stress is associated with flares in SLE and psychosomatic problems might affect quality of life and adherence to treatment.[32-33,49] Clinicians should evaluate psychological problems to comprehensively manage SLE patients. A study by Sakr et al showed that a psycho-educational program given to SLE patients for three months could improve SCl-90-R scores significantly, even though it did not affect disease activity.[50]

CONCLUSION

More than half of the subjects experienced psychosomatic disorders. Education level, psychosocial stressors, and disease activity level were found to be significantly associated with the occurrence of psychosomatic disorders in SLE patients during the COVID-19 pandemic. From this study, we suggest that these associated factors should be evaluated to avoid psychosomatic disorders during a pandemic. Psychoeducation can be given to SLE patients with higher risk of developing psychosomatic disorders: high education level, moderate-high psychosocial stressors, and moderate-very severe disease activity.

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CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any potential conflict of interest.

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