BMC Rheumatology

RESEARCH

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Cognitive impairment in systemic lupus erythematosus patients: prevalence and its association with quality of life

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Abstract

Background Cognitive impairment among patients with systemic lupus erythematosus (SLE) can significantly impact quality of life (QoL). This study aimed to determine the prevalence of cognitive impairment in SLE patients using the Montreal Cognitive Assessment Indonesian version (MoCA-INA) and to assess its association with QoL.

Methods This was a cross-sectional study of SLE patients from the outpatient clinic at Cipto Mangunkusumo Hospital, Jakarta. Data collected included patient characteristics, MoCA-INA scores, the LupusQoL questionnaire, and the Hospital Anxiety and Depression Scale (HADS) scores. The independent T-test or Mann-Whitney U test was used to analyze the association between categorical independent variables and LupusQoL, while Spearman or Pearson correlation tests were used to examine the association between numerical independent variables and QoL. Other factors potentially associated with QoL — including disease duration, age, education level, comorbidities, disease activity, organ involvement, steroid dose, immunosuppressant medication, anxiety, and depression — were also assessed. A p-value < 0.05 was considered statistically significant.

Results Of the 116 subjects, 112 (96.6%) were female, with a mean age of 34.41 (± 10.15) years. Most participants had completed secondary education, were receiving corticosteroids, and had been prescribed hydroxychloroquine. The median MEX-SLEDAI score was 2.75 (range 0–6), and the most common organ involvements were mucocutaneous (90.5%) and musculoskeletal (91.4%) manifestations. The prevalence of cognitive impairment in SLE patients was 57.8%, with most patients experiencing mild cognitive impairment (98.5%). There was no significant difference in QoL between SLE patients with and without cognitive impairment ($p = 0.750$). Disease duration ($r = 0.24$, $p = 0.011$), anxiety ($p < 0.001$), and depression ($p = 0.003$) were significantly associated with QoL among SLE patients.

Conclusions More than half of the subjects experienced cognitive impairment. However, there was no significant difference in QoL between SLE patients with and without cognitive impairment.

Clinical trial number Not applicable.

Keywords Systemic lupus erythematosus, Cognitive impairment, Quality of life

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Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects multiple organs, including the neuropsychiatric system [1, 2]. Cognitive impairment is one of the manifestations of neuropsychiatric systemic lupus erythematosus (NPSLE). It is more common in SLE patients with NPSLE compared to those without NPSLE, and more prevalent in SLE patients than in healthy controls [3]. Cognitive impairment is defined as a significant deficit in one or more cognitive functions, including attention, reasoning, executive skills (e.g., planning, organizing, sequencing), memory (e.g., learning, recall), visuospatial processing, language (e.g., verbal fluency), and psychomotor speed. Cognitive impairment can be debilitating and significantly affect quality of life (QoL), yet it remains underdiagnosed [4, 5]. Several studies have reported that the prevalence of cognitive impairment in SLE varies widely, ranging from 3 to 80% [6–8]. This variation is due to several factors, including differences in the populations assessed and the lack of standardized screening tools [6].

Cognitive impairment has been reported to have a major impact on the QoL of patients with systemic lupus erythematosus (SLE). Quality of life encompasses aspects of physical, mental, and social health, which are influenced by life experiences and expectations. People with SLE generally have a lower QoL compared to healthy individuals and patients with other chronic diseases [9]. Mortality rates in SLE patients have decreased, and the focus of care is now shifting toward enhancing patients' Health-Related Quality of Life (HRQoL) [10]. Quality of life in SLE patients is influenced by factors such as age, socioeconomic status, education level, depression, kidney involvement, skin involvement, comorbidities, disease duration, and physical activity [11–13]. Severe cognitive impairment can affect a patient's QoL in daily life, social interactions, education, and work [9]. Early screening for cognitive impairment in SLE patients can allow for earlier intervention [3], potentially improving both QoL and outcomes for these patients [9].

This study aimed to determine the prevalence of cognitive impairment among SLE patients and to explore the relationship between cognitive impairment and QoL using the Montreal Cognitive Assessment Indonesian version (MoCA-INA) and the Lupus Quality of Life (Lupus QoL) instruments. To our knowledge, no published study in Indonesia has assessed the association between cognitive impairment and QoL using both tools.

Methods

This was a cross-sectional study conducted at the outpatient clinic of Cipto Mangunkusumo Hospital in Jakarta, Indonesia, in May 2024. SLE patients who met the inclusion and exclusion criteria were recruited consecutively. The inclusion criteria were SLE patients aged 18 to 59 years, diagnosed with SLE according to the ACR/EULAR 2019 [14] or SLICC criteria [15]. The exclusion criteria included patients who could not read or write, had neurological disorders not related to SLE (such as a history of central nervous system infection, brain tumor, malignancy or metastasis, stroke with severe vascular cognitive impairment, head trauma, brain surgery, or brain hemorrhage), SLE overlap syndrome, or were not willing to participate in the study.

This study analyzed association between cognitive impairment as an independent variable and QoL among SLE patients as a dependent variable. Other confounding factors that might affect QoL (age, education level, disease duration, disease activity, comorbidity, organ involvement, steroid dose, immunosuppressant medications, anxiety, and depression) were also assessed. The data collected included patient characteristics (age, gender, comorbidities, education level, SLE organ involvement, SLE disease activity, use of corticosteroids and other immunosuppressants, and disease duration), MoCA-INA [16], Lupus QoL [17], and the Hospital Anxiety and Depression Scale (HADS) [18] to assess anxiety or depression that might affect QoL. Sampling was performed through interviews and secondary data collection from medical records. Data on SLE disease activity were assessed using the Mexican Version of the Systemic Lupus Erythematosus Disease Activity Index (MEX-SLEDAI) score [19]. MEX-SLEDAI is a simplified version of SLEDAI without the immunological tests, which makes the index cheaper to administer [20, 21].

To assess cognitive function, the MoCA-INA questionnaire was used. The MoCA is a sensitive cognitive screening test for detecting mild cognitive impairment and has been validated in Indonesia since 2010 under the name MoCA-INA. Subjects were considered to have cognitive impairment if their MoCA-INA score was below 26 points, with severity categorized as mild (18–25 points), moderate (10–17 points), and severe (under 10 points) [16].

The Lupus QoL questionnaire was used in this study to assess the QoL of SLE patients. The Lupus QoL is a 34-item, SLE-specific, health-related QoL measure. It consists of eight domains: physical health (8 items), pain (3 items), planning (3 items), intimate relationships (2 items), burden to others (3 items), emotional health (6 items), body image (5 items), and fatigue (4 items). The score ranges from 0 (worst QoL) to 100 (best QoL). This questionnaire was developed and validated by McElhone et al. [22] and has been translated and validated in Indonesia by Anindito et al. [17].

Symptoms of anxiety and depression were assessed using the HADS questionnaire. The HADS is a self-reporting measure consisting of 14 items, seven of which

assess anxiety and the remaining seven assess depression. Anxiety and depression were defined as an HADS score of 8 or more in the respective domains. The Indonesian version of the HADS questionnaire is a reliable and valid instrument. It has been used in the SLE population [18].

The protocol was reviewed and approved by the Ethics Committee of the Faculty of Medicine, University of Indonesia (KET-397/UN2.F1/ETIK/PPM.00.02/2024). All patients provided written informed consent before study enrollment. Clinical trial number: not applicable.

The sample size was determined using a formula for comparing the means of two independent groups to assess the association between cognitive impairment and QoL, with QoL score as the primary endpoint. Standard deviation (S) used was 13.2 from study by Monahan et al. [4]. Assuming a two-sided type I error rate (α) of 5% and a type II error rate (β) of 20% (80% power) with effect size (x1-x2) was 7, a total sample of 112 patients was required.

$$\mathrm{n1} = \mathrm{n2} = 2\left(\frac{[\mathrm{Z}\alpha + \mathrm{Z}\beta]\,\mathrm{S}}{\mathrm{x1} - \mathrm{x2}}\right)^2$$

The collected data were processed using the IBM SPSS Statistics for Windows, Version 20.0, Armonk, NY: IBM Corp. Frequencies and percentages were used to display descriptive data. Because the sample size was more than 50 subjects, the Kolmogorov – Smirnov test was performed to verify that the sample data were normally distributed. The difference in QoL between SLE patients with and without cognitive impairment was analysed using the independent t-test if the data were normally distributed, or the Mann-Whitney U test if the data were not normally distributed. Spearman or Pearson correlation tests were used to examine the association between numerical independent variables and QoL. Pearson correlation was used if the data were normally distributed. Other factors potentially associated with QoL — including disease duration, age, education level, comorbidities, organ involvement, disease activity, steroid dose, immunosuppressant medications, anxiety, and depression — were also assessed. Multivariate analysis was conducted using linear regression to assess the effect of confounding variables on the association between cognitive impairment and QoL. A p-value < 0.05 was considered statistically significant.

Results

Demographic characteristic

A total of 116 SLE patients participated in this study. Of these, 112 (96.6%) were female, with a mean (± SD) age of 34.41 ± 10.15 years. The education levels of the study subjects were as follows: primary education (11.2%), secondary education (50%), and tertiary education (38.8%).

The median (IQR) duration of SLE diagnosis was 52 (16.75–109.50) months, and 41 (35.3%) subjects had comorbidities. The comorbidities included hypertension, diabetes mellitus, chronic kidney disease, cardiovascular disease, chronic liver disease, and pulmonary disease. The median (IQR) SLE disease activity score was 2.75 (0; 6). Organ involvements included musculoskeletal (91.4%), mucocutaneous (90.5%), renal (39.7%), hematology (26%), and neuropsychiatric (19.8%). Most subjects were treated with corticosteroids (89.7%) for more than one year (81.9%) and took hydroxychloroquine (68.1%). The median (IQR) last dose of corticosteroid was 4 (1.1–4) mg methylprednisolone per day. Other steroid-sparing agents included mycophenolate sodium (41.4%), azathioprine (16.4%), methotrexate (5.2%), and cyclosporine (3.4%). Additionally, 56 subjects (48.3%) tested positive for antiphospholipid antibodies. Twenty-four (20.7%) subjects had depression, and 44 (37.9%) subjects had anxiety.

Prevalence of cognitive impairment

Cognitive function was assessed in 116 subjects using the validated MoCA-INA questionnaire [14]. Of these, 67 subjects (57.8%) exhibited cognitive impairment. Among those with cognitive impairment, 66 subjects (98.5%) had mild cognitive impairment, while one subject (1.5%) had moderate cognitive impairment.

Association between cognitive impairment and quality of life

Median (IQR) QoL was 79.88 (65.5–87.02). The median (IQR) for each domain of QoL were as follows: 78.1 (68.75–89.82) for physical health, 75 (66.66–91.6) for pain, 87.65 (75–100) for planning, 100 (75–100) for intimate relationships, 75 (50–91.6) for burden to others, 79.05 (59.37–87.5) for emotional well-being, 85 (66.25–98.75) for body image, and 75 (56.25–87.5) for fatigue.

Bivariate analysis using the Mann-Whitney U test (Table 1) showed no significant difference in QoL between SLE patients with and without cognitive impairment ($p = 0.750$). Other factors potentially associated with QoL among SLE patients were also analyzed. Disease duration ($r = 0.24$, $p = 0.011$), anxiety ($p < 0.001$), and depression ($p = 0.003$) were significantly associated with QoL, while age ($r = 0.18$, $p = 0.058$), SLE disease activity (r = -0.15, $p = 0.117$), comorbidities, steroid dose (r = -0.10, $p = 0.291$), immunosuppressant medications, organ involvement, and education level were not significantly associated. From multivariate analysis with linear regression, only anxiety showed significant association with QoL (β: -14.67, 95% CI: -20.49 to -8.86, $p < 0.001$).

Associations between cognitive impairment, anxiety, depression, disease duration, age, disease activity, comorbidities, steroid dose, immunosuppressant medications,

Table 1 Bivariate and multivariate analysis of factors associated with quality of life among SLE patients

Variables	Lupus quality of life score							
	Bivariate analysis				Multivariate analysis***			
	Median (Q1-Q3)	*r*	*p*	β coefficient	*p*	95% CI		*R* square
						Lower	Upper	
Cognitive impairment*								0.38
Yes	80.35 (65.67–85.83)	-	0.750					
No	77.25 (65.42–88.48)							
Depression*								
Yes	63.22 (47.02–83.74)	-	0.003****	-6.47	0.058	-13.17	0.23	
No	81.06 (71.11–87.20)							
Anxiety*								
Yes	65.33 (50.77–77.18)	-	< 0.001****	-14.67	< 0.001****	-20.49	-8.86	
No	84.20 (76.85–89.24)							
Disease duration**	-	0.24	0.011****	0.03	0.165	-0.01	0.07	
Age**	-	0.18	0.058	0.14	0.288	-0.12	0.40	
Disease activity**	-	-0.15	0.117	-0.17	0.709	-1.08	0.74	
Comorbidities*								
Yes	81.51 (62.44–88)		0.680					
No	77.99 (65.67–86.75)							
Steroid dose**	-	-0.10	0.291					
Immunosuppressants medications								
Hydroxychloroquine*								
Yes	80.86 (65.40–86.75)	-	0.790					
No	78.16 (69.56–87.76)							
Mycophenolate sodium*								
Yes	76.40 (54.52–85.49)	-	0.073					
No	81.49 (67.93–88.35)							
Azathioprine*								
Yes	78.16 (65.44–89.70)	-	0.573					
No	80 (65.53–86.77)							
Methotrexate*								
Yes	64.73 (51.56–86.28)	-	0.257					
No	80.18 (65.72–87.09)							
Cyclosporine*								
Yes	88.16 (73.50–89.24)	-	0.212	5.43	0.424	-7.97	18.82	
No	79.19 (65.41–86.62)							
Organ Involvement								
Musculoskeletal*								
Yes	80.18 (65.61–87.13)	-	0.387					
No	73.70 (62.93–84.29)							
Mucocutaneous*								
Yes	79.75 (65.42–86.94)	-	0.519					
No	81.51 (68.98–92.31)							
Renal*								
Yes	81.34 (70.80–87.17)	-	0.431					
No	78.39 (65.06–86.87)							
Hematology*								
Yes	83.50 (65.22–88.79)	-	0.577					
No	78.58 (65.56–85.88)							
Neuropsychiatric*								
Yes	80 (50.49–88.28)	-	0.452					
No	79.75 (67.07–86.77)							
Education level*								

Table 1 (continued)

Variables	Lupus quality of life score							
	Bivariate analysis				Multivariate analysis***			
	Median (Q1-Q3)	*r*	*p*	β coefficient	*p*	95% CI		*R* square
						Lower	Upper	
Primary	81.51 (59.05–91.16)	-	0.160	1.40	0.497	-2.68	5.48	
Secondary	77.48 (61.23–85.83)							
Tertiary	81.05 (66.83–89.02)							

*Mann Whitney U test, **Spearman test, ***linear regression, ****$p < 0.050$

organ involvement, and education level with each domain of QoL were further analyzed (Table 2). Anxiety showed a significant association with all domains of QoL. Meanwhile, depression showed a significant association with all domains of QoL, except for the fatigue domain ($p = 0.373$). Disease duration showed a significant association with burden to others ($r = 0.24$, $p = 0.011$), emotional health ($r = 0.28$, $p = 0.003$), and body image domain ($r = 0.20$, $p = 0.034$). Age showed a significant association with all domains of QoL, except pain ($p = 0.196$) and planning ($p = 0.752$). Mycophenolate mofetil was significantly associated with body image domain ($p = 0.008$), while musculoskeletal involvement was significantly associated with intimate relationship domain ($p = 0.030$).

There were also significant associations between SLE disease activity and the emotional (r = -0.22, $p = 0.016$) and fatigue domains (r = -0.21, $p = 0.022$), as measured by Spearman correlation. SLE disease activity was not associated with other domains of lupus QoL: physical health (r = -0.10, $p = 0.266$), pain (r = -0.10, $p = 0.299$), planning (r = -0.08, $p = 0.378$), intimate relationships ($r = 0.07$, $p = 0.427$), burden to others (r = -0.13, $p = 0.160$), and body image (r = -0.18, $p = 0.060$).

Factors associated with cognitive impairment

We also conducted additional analysis to identify factors associated with cognitive impairment (Table 3). The bivariate analysis revealed that age, comorbidities, renal involvement, and educational level had a p-value < 0.25 and were included in multivariate analysis using logistic regression. SLE patients with a lower educational level (primary or secondary) showed a higher proportion of cognitive impairment compared to those with a tertiary educational level [primary vs. tertiary; 4.48 (1.02–19.72), $p = 0.047$; secondary vs. tertiary, 3.54 (1.46–8.58), $p = 0.005$].

Discussion

According to our study, there was 57.8% SLE patients had cognitive impairment, with all but one patient experiencing mild cognitive impairment. There was no significant difference in QoL between SLE patients with and without cognitive impairment. However, from bivariate analysis, anxiety, depression, and disease duration were significantly associated with QoL among SLE patients.

The prevalence of cognitive impairment in SLE patients across studies varied due to heterogeneity in sociodemographics, comorbidities, screening tools, standard definitions, and research methods [3]. The proportion of subjects with cognitive impairment in our study was 57.8%, as assessed using the MoCA-INA screening tool. Previous studies using the MoCA tool have reported similar prevalences of cognitive impairment: 65.1% in Pakistan and 67.9% in China [23, 24], while the prevalence was lower in Malaysia (35%) [25]. There are many factors that can contribute to this difference, one of which may be related to the education levels of the subjects. The study conducted in Malaysia had a higher proportion of subjects with tertiary education compared to our study [25].

Although more than half of our subjects had cognitive impairment, most had mild cognitive impairment, and only one subject had moderate cognitive impairment. Mild cognitive dysfunction is common in SLE, but it is often not directly linked to the condition itself [26]. A systematic review and meta-analysis by Rayes et al. showed that the prevalence of cognitive impairment among SLE patients, using other screening tools, was 38% with the Comprehensive Battery (CB), 26% with the Automated Neuropsychological Assessment Metric (ANAM), and 23% with the Modified Mini-Mental State Exam (MMSE) [3]. A study from our hospital in 2011 using the MMSE found that 63.8% of SLE patients had cognitive impairment [8].

Most of the study subjects were female, with a mean (± SD) age of 34.41 (± 10.15) years. This is consistent with the epidemiology of SLE, where most cases occur among young or middle-aged women of reproductive age. In our study, half of the subjects had completed secondary education, while 11.2% had only completed primary education. These characteristics were similar to those in a previous study on QoL among SLE patients by Anindito et al., conducted at our hospital in 2015 [17]. Another study by Mizukami et al. on QoL among SLE patients in Hanoi showed a lower percentage of subjects with secondary education and a higher proportion with only primary education [27].

Table 2 Factors associated with each domain of quality of life among SLE patients

Variables	Total QoL	*p* value	Physical health	*p* value	Pain	*p* value	Planning	*p* value	Intimate relationship	*p* value	Burden to others	*p* value	Emotional health	*p* value	Body image	*p* value	Fatigue	*p* value
Cognitive Impairment*																		
Yes	80.35 (65.67–85.83)	0.750	81.20 (68.75–90.62)	0.200	83.3 (66.60–91.60)	0.500	83.3 (75–100)	0.120	100 (75–100)	0.890	75 (50–91.60)	0.410	79.10 (54.10–87.50)	0.730	85 (50–100)	0.880	75 (56.25–87.50)	0.810
No	77.25 (65.42–88.48)		78.10 (68.72–85.83)		75 (67.65–87.45)		91.66 (75–100)		100 (75–100)		75 (50–91.60)		75 (62.50–91.63)		80 (70–94)		75 (56.25–87.50)	
Anxiety*																		
Yes	65.33 (50.77–77.18)	< 0.001***	70.27 (62.50–80.42)	< 0.001***	75 (52.07–83.30)	< 0.001***	75 (58.30–91.60)	< 0.001***	75 (56.25–100)	0.001***	50 (27.07–75)	< 0.001***	58.3 (37.50–75)	< 0.001***	72.5 (46.25–85)	< 0.001***	62.25 (89.06–75)	< 0.001***
No	84.20 (76.85–89.24)		84.37 (75–90.62)		83.30 (75–91.82)		91.66 (83.30–100)		100 (87.35–100)		83.3 (75–98.67)		83.3 (75–93.30)		90 (75–100)		75 (62.50–87.50)	
Depression*																		
Yes	63.22 (47.02–83.74)	0.003***	70.27 (52.34–80.42)	0.008***	70.8 (41.60–89.52)	0.013***	75 (54.15–91.60)	0.004***	75 (40.62–100)	0.003***	50 (27.07–81.22)	0.007***	60.4 (34.45–86.50)	0.021***	72.5 (28.75–93.75)	0.041***	68.75 (40.62–87.50)	0.373
No	81.06 (71.11–87.20)		82.22 (69.51–90.60)		75 (75–91.60)		91.6 (75–100)		100 (75–100)		75 (58.30–91.64)		79.16 (70.80–90.57)		85 (70–100)		75 (62.12–81.62)	
Disease duration**	r 0.24	0.011***	r 0.14	0.132	r 0.11	0.249	r 0.10	0.298	r 0.12	0.249	r 0.24	0.011***	r 0.28	0.003***	r 0.20	0.034***	r 0.25	0.070
Age**	r 0.18	0.058	r 0.22	0.018***	r 0.12	0.196	r 0.03	0.752	r –0.19	0.043***	r 0.37	< 0.001***	r 0.29	0.002***	r 0.19	0.045***	r 0.19	0.042***
Disease activity**	r -0.15	0.117	r -0.10	0.266	r -0.10	0.299	r -0.08	0.378	r 0.07	0.427	r -0.13	0.160	r -0.22	0.016***	r -0.18	0.060	r -0.21	0.022***
Comorbidities*																		
Yes	81.51 (62.44–88)	0.680	78.10 (75–91.60)	0.731	75 (58.30–91.60)	0.342	83.30 (75–100)	0.691	100 (75–100)	0.468	75 (54.15–93.20)	0.133	83.30 (54.15–91.68)	0.377	90 (75–100)	0.210	75 (56.22–87.50)	0.807
No	77.99 (65.67–86.75)		78.10 (68.70–87.50)		75 (75–91.60)		91.60 (75–100)		100 (75–100)		75 (41.60–83.30)		75 (62.50–87.50)		80 (65–95)		75 (56.25–87.50)	
Steroid dose**	r -0.10	0.291	r -0.06	0.541	r -0.11	0.236	r -0.12	0.213	r 0.04	0.710	r -0.09	0.332	r -0.15	0.102	r -0.18	0.051	r -0.14	0.120
Immunosuppressant medication*																		
Hydroxychloroquine																		

Table 2 (continued)

Variables	Total QoL	*p* value	Physical health	*p* value	Pain	*p* value	Planning	*p* value	Intimate relationship	*p* value	Burden to others	*p* value	Emotional health	*p* value	Body image	*p* value	Fatigue	*p* value
Yes	80.86 (65.40–86.75)	0.790	78.12 (68.75–90.60)	0.671	75 (66.60–91.60)	0.878	83.70 (75–100)	0.711	100 (75–100)	0.682	75 (41.60–91.60)	0.860	75 (41.60–91.60)	0.447	80 (65–100)	0.530	70 (56.25–87.50)	0.386
No	78.16 (69.56–87.76)		78.10 (68.75–87.50)		75 (75–87.45)		91.60 (75–100)		100 (75–100)		75 (50.36–91.60)		75 (50.36–91.60)		85 (75–95)		75 (62.50–87.50)	
Mycophenolate mofetil																		
Yes	76.40 (54.52–85.49)	0.073	78.10 (68.75–87.50)	0.471	75 (58.30–91.60)	0.139	83.30 (75–100)	0.098	100 (75–100)	0.778	75 (50–83.30)	0.228	75 (55.15–86.50)	0.173	75 (41.25–90)	0.008***	68.77 (51.56–81.25)	0.169
No	81.49 (67.93–88.35)		78.11 (68.75–90.60)		78.10 (68.75–87.50)		91.60 (75–100)		100 (75–100)		75 (43.70–91.67)		79.16 (66.60–91.64)		87.50 (75–100)		75 (60.62–87.50)	
Azathioprine																		
Yes	78.16 (65.44–89.70)	0.573	78.10 (65.60–90.62)	0.866	91.60 (75–91.70)	0.072	100 (75–100)	0.351	100 (75–100)	0.334	75 (33.33–91.60)	0.845	75 (58.30–87.50)	0.275	90 (70–95)	0.299	75 (56.25–87.50)	0.744
No	80 (65.53–86.77)		78.10 (68.75–89.05)		75 (66.60–90.62)		83.3 (75–100)		100 (75–100)		75 (50–91.60)		79.10 (62.50–89.55)		80 (65–100)		75 (56.25–84.62)	
Methotrexate																		
Yes	64.73 (51.56–86.28)	0.257	68.70 (60.93–87.50)	0.179	66.85 (37.52–81.25)	0,175	75 (64.52–93.70)	0.221	77 (18.75–100)	0.136	79.15 (37.45–100)	0.629	77.05 (36.45–87.50)	0.866	77.5 (52.50–85)	0.399	59.35 (40.62–82.77)	0.254
No	80.18 (65.72–87.09)		78.10 (68.75–90.60)		75 (66.69–91.60)		91.60 (75–100)		100 (75–100)		75 (50–91.60)		79.05 (61.45–87.50)		85 (65–100)		75 (56.25–87.50)	
Cyclosporine																		
Yes	88.16 (73.50–89.24)	0.212	78.11 (73.37–89.84)	0.660	79.15 (75–95.82)	0.500	91.65 (77.07–100)	0.521	100 (81.25–100)	0.457	83.30 (39.57–95.82)	0.522	83.33 (75–93.94)	0.426	85 (76.25–90)	0.963	81.25 (75–87.50)	0.181
No	79.19 (65.41–86.62)		78.10 (68.75–89.82)		75 (66.61–91.60)		87.65 (75–100)		100 (75–100)		75 (50–91.60)		79.05 (58.30–87.50)		85 (65–100)		75 (56.25–86.06)	
Organ involvement*																		
Musculoskeletal																		

Table 2 (continued)

Variables	Total QoL	*p* value	Physical health	*p* value	Pain	*p* value	Planning	*p* value	Intimate relationship	*p* value	Burden to others	*p* value	Emotional health	*p* value	Body image	*p* value	Fatigue	*p* value
Yes	80.18 (65.61–87.13)	0.387	78.10 (68.70–90.60)	0.738	75 (66.64–91.60)	0.917	83.31 (75–100)	0.727	100 (75–100)	0.030***	75 (50–91.60)	0.212	79.10 (5.30–91.60)	0.375	82.50 (65–100)	0.680	75 (56.25–87.50)	0.438
No	73.70 (62.93–84.29)		82.77 (65.55–87.12)		75 (70.82–93.74)		91.60 (75–100)		75 (43.75–100)		62.50 (25–79.15)		75 (68.72–80.19)		87.50 (78–95)		66.25 (54.65–76.56)	
Mucocutaneous																		
Yes	79.75 (65.42–86.94)	0.519	78.10 (68.75–89.05)	0.766	75 (66.68–91.60)	0.706	91.60 (75–100)	0.556	100 (75–100)	0.821	75 (50–83.30)	0.288	79.10 (58.30–87.50)	0.305	80 (65–95)	0.156	75 (56.25–84.62)	0.794
No	81.51 (68.98–92.31)		75 (62.50–90.62)		75 (58.30–100)		83.30 (75–100)		87.50 (75–100)		91.60 (33.30–100)		75 (75–100)		95 (75–100)		75 (50–87.50)	
Renal																		
Yes	81.34 (70.80–87.17)	0.431	78.10 (68.75–90.60)	0.957	75 (75–91.66)	0.275	83.30 (75–100)	0.923	100 (75–100)	0.121	75 (56.40–91.60)	0.836	79.13 (73.95–88.52_	0.630	82.50 (68.75–95)	0.743	75 (56.25–87.50)	0.463
No	78.39 (65.06–86.87)		78.11 (68.75–88.27)		75 (58.60–91.60)		91.60 (75–100)		100 (75–100)		75 (41.60–91.61)		77 (54.14–88.52)		85 (65–100)		82.50 (68.75–95)	
Hematology																		
Yes	83.50 (65.22–88.79)	0.577	75 (65.60–87.50)	0.637	83.30 (75–91.70)	0.227	91.60 (75–100)	0.791	100 (75–100)	0.638	75 (33.33–91.60)	0.685	75 (58.33–87.50)	0.221	88 (70–95)	0.637	70 (56.26–87.50)	0.863
No	78.58 (65.56–85.88)		78.10 (68.75–90.60)		75 (66.60–83.30)		83.33 (75–100)		100 (75–100)		75 (50–91.60)		79.16 (60.40–91.63)		80 (65–100)		75 (56.25–81.25)	
Neuropsychiatric																		
Yes	80 (50,49–88,28)	0,452	75 (65.60–90.60)	0.523	83.30 (50–91.60)	0.858	83.30 (66.60–100)	0.365	87.50 (37.50–100)	0.086	75 (41.60–91.60)	0.732	75 (45.80–91.60)	0.190	85 (55–100)	0.972	70 (56.25–87.50)	0.884
No	79,75 (67,07–86,77)		78.10 (68.75–89.05)		75 (66.68–91.60)		91.60 (75–100)		100 (75–100)		75 (50–91.60)		79.16 (67.05–87.50)		85 (67.50–97.50)		75 (56.25–84.62)	
Education level*																		
Primary	81.51 (59.05–91.16)	0.160	81.20 (65.62–90.61)	0.806	83.30 (66.65–95.93)	0.245	91.60 (75–100)	0.690	100 (75–100)	0.978	75 (70.80–91.65)	0.210	83.30 (75–93.70)	0.110	90 (72.50–100)	0.083	81.20 (65.62–93.72)	0.138

Table 2 (continued)

Variables	Total QoL	*p* value	Physical health	*p* value	Pain	*p* value	Planning	*p* value	Intimate relationship	*p* value	Burden to others	*p* value	Emotional health	*p* value	Body image	*p* value	Fatigue	*p* value
Secondary	77.48 (61.23–85.83)		78.10 (68.70–90.60)		75 (58.60–83.30)		83.50 (75–100)		100 (75–100)		75 (41.60–83.30)		75 (48.95–84.37)		77.50 (48.75–95)		68.72 (50–81.37)	
Tertiary	81.05 (66.83–89.02)		78.10 (70.27–87.50)		83.30 (70.85–91.63)		83.33 (75–100)		100 (75–100)		75 (58.30–93.2)		75 (67.05–91.60)		90 (72.50–100)		75 (61–87.50)	

*Mann Whitney U test, **Spearman test, *** $p < 0.050$

The median (IQR) duration of SLE diagnosis in our study was 52 (16.75–109.5) months. This was similar to a study by Wang et al. assessing QoL among SLE patients in China, which reported a duration of 4.8 (± 4.4) years [28]. The median MEX-SLEDAI in our study was 2.75 (0–6), which was comparable to a study by Etchegaray-Morales et al. assessing QoL among SLE patients in Mexico, which reported a median (IQR) MEX-SLEDAI of 2.3 (0–13) [29]. The median (IQR) corticosteroid dose in our study was 4 (1.1–4) mg methylprednisolone per day, while a study by Calderón et al. reported a median (IQR) corticosteroid dose of 10 (2–25) mg methylprednisolone per day [30].

The median QoL score of SLE patients in our study was 79.88 (65.5–87.02) using the lupusQOL. This result was higher than those reported in studies among SLE patients in the United States (47.3) [31], Iran (65.5) [12], Mexico (69) [19], Asia (70.81) [32], and the United Kingdom (71.07) [31]. QoL domains are influenced by various factors across different countries. Disease activity, in particular, can impact QoL among SLE patients [33]. If SLE disease activity remains consistently low, it may improve QoL [34]. The median (IQR) SLE disease activity in our study was 2.75 (0–6).

In our study, the QoL domains with the worst scores were "burden to others," followed by "fatigue" and "pain," while the highest score was for "intimate relationships." This result was similar to a study by García-Carrasco et al. using the same questionnaire (Lupus QoL), which reported that "burden to others" had the lowest score [19]. Another study by Etchegaray-Morales et al. [29] also showed that "burden to others," "fatigue," and "emotional" domains had the worst scores. Hashemi et al. reported that the domain with the worst scores among SLE patients in Iran was "emotional" [12].

We did not find a significant association between cognitive impairment and QoL for the total score or the score of each domain. A study by Calderon et al. among SLE patients with a median age of 35 years found no significant association between learning deficits, visuospatial memory, or attention and QoL in SLE patients. However, executive dysfunction was associated with both the physical and mental health components of QoL in SLE patients with depression. This study used the Cambridge Neuropsychological Test Automated Battery (CANTAB) to assess cognitive function and the 12-item Medical Outcomes Study (MOS) Short Form Health Survey version 2 (SF-12v2) to assess QoL [30]. Monahan et al. found a weak relationship between cognitive impairment and QoL in patients with SLE. This study used the SF-36 instrument to assess QoL [4]. Another study by Raghunath et al. found significant association between cognitive impairment measured by 1-hour conventional neuropsychological test battery and QoL measured by

Table 3 Bivariate and multivariate analysis of factors associated with cognitive impairment among SLE patients

Variables	Cognitive impairment					
	Bivariate analysis				Multivariate analysis*****	
	Yes	No	Crude OR	*p* value	Adjusted OR	*p* value
Depression, n (%)*	13 (54.17)	11 (45.83)	0.83 (0.34–2.05)	0.867		
Anxiety, n (%)*	24 (54.54)	20 (45.45)	0.81 (0.38–1.73)	0.723		
Disease duration, months, Median (Q1-Q3) ****	48 (15–11)	56 (24–109.50)	-	0.467		
Age, years, Mean (SD) ***	35.69 (10.80)	32.67 (9.02)	-	0.115	1.03 (0.98–1.07)	0.271
Disease activity, Median (Q1-Q3) ****	0 (0–2)	0 (0–4)	-	0.629		
Comorbidities, n (%)*	28 (68.29)	13 (31.71)	1.99 (0.90–4.42)	0.133	0.53 (0.21–1.36)	0.186
Steroid dose, Median (Q1-Q3) ****	4 (0.60–4)	4 (1.55–6)	-	0.689		
Immunosuppressants medications						
Hydroxychloroquine, n (%)*	47 (59.49)	32 (40.51)	1.25 (0.57–2.74)	0.725		
Mycophenolate sodium, n (%)*	27 (56.25)	21 (43.75)	0.90 (0.43–1.90)	0.932		
Azathioprine, n (%)**	11 (57.89)	8 (42.10)	1.01 (0.37–2.72)	1.000		
Methotrexate, n (%)*	4 (66.67)	2 (33.33)	1.49 (0.26–8.49)	1.000		
Cyclosporine, n (%)	0 (0)	4 (100)	-	-		
Organ Involvement						
Musculoskeletal, n (%)**	62 (58.49)	44 (41.51)	1.41 (0.38–5.16)	0.741		
Mucocutaneous, n (%)**	60 (57.14)	45 (42.86)	0.76 (0.21–2.76)	0.758		
Renal, n (%)*	23 (50)	23 (50)	0.59 (0.28–1.26)	0.238	2.01 (0.85–4.75)	0.113
Hematology, n (%)*	17 (54.84)	14 (45.16)	0.85 (0.37–1.95)	0.863		
Neuropsychiatric, n (%)*	11 (47.83)	12 (52.17)	0.61 (0.24–1.52)	0.400		
Education level, n (%)*						
Primary	10 (76.92)	3 (23.08)	5.00 (1.21–20.71)	0.026	4.48 (1.02–19.72)	0.047******
Secondary	39 (67.24)	19 (32.76)	3.08 (1.37–6.92)	0.007	3.54 (1.46–8.58)	0.005******
Tertiary	18 (40)	27 (60)	Refference		Refference	

*Chi square, **Fisher exact, *** Independent T test, ****Mann Whitney U test, *****logistic regression, ****** $p < 0.050$

the Medical Outcomes Study 36-item short form health survey (SF-36v2) [35]. Several factors might explain the differing results between studies: variability in the tools used to assess cognitive impairment and QoL, the effect of SLE and its treatment, and how patients compensate for their cognitive impairment [4]. A systematic review by Mendelsohn et al. showed that cognitive impairment in SLE patients was negatively related to QoL. Unlike our study, none of the studies included in the systematic review used both MoCA and LupusQoL to assess cognitive impairment and QoL [9]. Mild to moderate cognitive impairment is unlikely to affect QoL, with only severe cognitive impairment being associated with poor QoL. In our study, most subjects had mild cognitive impairment, and only one subject exhibited moderate cognitive impairment.

Quality of life in SLE patients can be influenced by various factors. Disease activity correlates negatively with QoL among SLE patients [29, 36]. Although we did not find a significant association between disease activity and QoL, a negative correlation was found between disease activity and the emotional and fatigue domains. Conti et al. in Italy found that patients with high disease activity (SLEDAI-2 K ≥ 4) had poor QoL compared to patients with low disease activity (SLEDAI-2 K < 4), with significant differences in the domains of physical health, planning, burden to others, and fatigue [37]. Carrión-Nessi et al. concluded that disease activity was negatively correlated with LupusQoL domains, except for intimate relationships and burden to others [38]. In contrast, Yilmaz-Oner et al. in Turkey found no association between disease activity and QoL, suggesting that other factors might affect QoL, especially among SLE patients with clinically inactive or mildly active disease [39]. The association between disease activity and QoL in various studies provides diverse or heterogeneous results. This variability may arise from differences in research design, the heterogeneity of the disease, and the varying scoring methods used to evaluate disease activity and its fluctuating status [36].

In this study, from bivariate analysis, a significant relationship was found between depression and anxiety with the total QoL score and in all QoL domains, except in the fatigue domain, where there was no significant relationship with depression. Etchegarai-Morales et al. found that depression correlated with poorer QoL (r = -0.61; $p < 0.005$) [29]. Chen et al. found that anxiety was associated with QoL among SLE patients [40]. From regression analysis, we found only anxiety was significantly associated with QoL ($p < 0.001$). Study by Ceccarelli et al. found that mood disorder, particularly depression, and fibromyalgia were the main determinants of worse QoL [41].

We found a positive correlation between the disease duration and QoL. This contrasts with a study by Hashemi et al., which found that disease duration was negatively correlated with QoL among SLE patients in Iran [12].

We found a significant association between musculoskeletal involvement with QoL among SLE patients. This result was different from study by Muhammed et al. which showed that neuropsychiatric manifestations could negatively affect QoL [42]. We also did not find significant association between comorbidities with QoL among SLE patients, while study by Aljohani et al. found that comorbidities were significantly associated with QoL [43].

There were some limitations in this study. It was a single-center, cross-sectional study. Another limitation was that most patients had low levels of disease activity, so the results might not represent patients with higher levels of disease activity, which could have a greater effect on QoL. A further limitation was that we did not assess socioeconomic status or social support, which might also affect QoL. Study by Herna´ndez-Ledesma et al. found that socioeconomic status was one of factors that affect QoL among SLE patients in Mexico [44].

Conclusion

The prevalence of cognitive impairment in SLE patients was 57.8%, with most subjects having mild cognitive impairment (98.5%). There was no significant difference in QoL between SLE patients with and without cognitive impairment. From bivariate analysis, disease duration, anxiety, and depression were significantly associated with QoL among SLE patients. Age, disease activity, comorbidities, steroid dose, immunosuppressant medications, organ involvement, and education level did not show significant association with QoL among SLE patients. However, there was a significant association between SLE disease activity and the emotional and fatigue domains of QoL. The limitation of this study is its cross-sectional design, and the socioeconomic factors related to the QoL of SLE patients were not assessed. A prospective cohort study that includes other socioeconomic factors could be conducted in the future to provide stronger evidence.

Acknowledgements
We would like to thank Utami Susilowati for her assistance in data analysis. We also thank Reni Febriani, Elyani, and Putri Aisyah for their assistance in data collection.

Author contributions
MG, AW, RE, SK, SM, RMSAKW, PS contributed to conceptualization; SK, HS, RMSAKW, AR contributed to methodology; MG, AW, RE, SK, SM, PP contributed to investigation; MG, SK, NKS contributed to formal analysis; MG, AW, RE, SK contributed to writing the original draft; SM, PS, HS, RMSAKW, PP, NKS, AR contributed to editing the manuscript. All authors read and approved the final manuscript.

Funding
This publication was supported by a PUTI grant from the University of Indonesia (NKB-57/UN2.RST/HKP.05.00/2024).

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

Declarations

Ethics approval and consent to participate
This study was approved by the Research Ethics Committee of the Faculty of Medicine, University of Indonesia (KET-397/UN2.F1/ETIK/PPM.00.02/2024) on 13 March 2024. The study was carried out in accordance with the ethical principles for medical research in humans of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Consent for publication
There is no individual or identifiable data within this manuscript.

Competing interests
The authors declare no competing interests.

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Received: 27 November 2024 / Accepted: 18 March 2025
Published online: 28 March 2025

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