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Research Article

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SLICC/ACR Damage Index (SDI) Score in Systemic Lupus Erythematosus Patients and its Associated Factors

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Abstract

Background: *Systemic lupus erythematosus (SLE) is a chronic autoimmune disease associated with irreversible organ damage. The Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) is widely used to quantify accumulated damage. This study aimed to determine the prevalence and associated factors of organ damage among SLE patients in a Malaysian tertiary centre.*

Methods: *A cross-sectional study was conducted at Hospital Pakar Universiti Sains Malaysia between 2018 and 2025. Patients fulfilling SLE classification criteria with disease duration ≥6 months were included. Data were obtained from medical records. Organ damage was assessed using the SDI. Logistic regression analyses were performed to identify associated factors.*

Results: *A total of 89 patients were included, with a mean age of 38.9 years and mean disease duration of 9.1 years. The majority were female (94.4%) and Malay (86.5%). Organ damage (SDI ≥1) was present in 47.2% of patients. The most common domains were ocular (12.4%) and diabetes-related damage (7.9%). Multivariable analysis identified diabetes mellitus (adjusted OR 15.3, 95% CI 1.77–132.32, p=0.013) and cyclophosphamide use (adjusted OR 5.37, 95% CI 1.89–15.30, p=0.002) as independent predictors.*

Conclusion: *Nearly half of SLE patients had irreversible organ damage. Diabetes mellitus and cyclophosphamide exposure were the strongest predictors. Optimizing comorbidity control and minimizing treatment toxicity are crucial to reduce long-term damage.*

Keywords: Systemic Lupus Erythematosus, SLICC Damage Index, Organ Damage, Cyclophosphamide, Diabetes Mellitus, Malaysia

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease characterized by heterogeneous clinical manifestations and long-term morbidity. Despite improved survival, accumulated irreversible organ damage remains a major determinant of poor outcomes and mortality [1,2].

The Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) was developed to quantify irreversible organ damage persisting for at least six months. Higher SDI scores are strongly associated with increased mortality [3,4].

Damage accrual in SLE is multifactorial, resulting from disease activity, comorbidities, and treatment-related toxicities. Identifying modifiable and non-modifiable risk factors is essential to improve long-term outcomes [5].

In Malaysia, data on SDI and its determinants remain limited. This study aimed to evaluate the prevalence and associated factors of organ damage among SLE patients in Hospital Pakar Universiti Sains Malaysia.

2. Methods

2.1. Study Design and Population

This cross-sectional study was conducted at the Systemic Lupus Erythematosus (SLE) clinic, Hospital Universiti Sains Malaysia (HPUSM), Kubang Kerian, Kelantan. The source population comprised all patients diagnosed with SLE and followed up at the clinic between 2018 and 2025. Patients were eligible if they fulfilled ≥4 criteria from either the 1997 American College of Rheumatology (ACR) or the 2019 EULAR/ACR classification criteria, had a disease duration ≥6 months, and were aged >12 years. Pregnant patients were excluded.

2.2. Sampling and Recruitment

Convenience sampling was used. Based on hospital records, approximately 140 SLE patients were followed up during the study period. All eligible patients attending the clinic during data collection were recruited until the required sample size was achieved.

2.3. Data Collection

Sociodemographic and clinical data were extracted from medical records, including age, sex, ethnicity, comorbidities, and disease duration. Laboratory data included antinuclear antibody (ANA) titres, anti–double-stranded DNA (anti-dsDNA), lupus anticoagulant (LA), and anti-cardiolipin antibodies (ACL). ANA titres were categorised as low (≤1:80) or high (≥1:160), while other autoantibodies were classified as positive or negative.

Medication exposure data were obtained from clinical and pharmacy records, including oral prednisolone (≥1 mg/kg/day for >2 weeks) and immunosuppressive agents (mycophenolate mofetil/mycophenolic acid, cyclosporine A, azathioprine, and hydroxychloroquine). Complement levels (C3 and C4) were calculated as the mean of all available values from routine monitoring during follow-up.

2.4. Assessment of Organ Damage

Organ damage was assessed using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR DI). Damage was defined as irreversible change persisting for ≥6 months, irrespective of cause, including treatment-related damage. Patients were categorised into those with organ damage (SDI ≥1) and those without damage (SDI = 0).

2.5. Statistical Analysis

Data were analysed using IBM SPSS Statistics version 30. Baseline characteristics were summarised descriptively, with categorical variables presented as frequencies and percentages and continuous variables as mean (standard deviation). Associations with organ damage were evaluated using logistic regression, with results reported as odds ratios (ORs) and 95% confidence intervals (CIs). Statistical significance was set at $p<0.05$.

2.6. Ethical Considerations

Ethical approval was obtained from the Human Research Ethics Committee of Universiti Sains Malaysia (JEPeM; USM/JEPeM/KK/25070605). Approval of accessing medical records was granted by the Hospital Director. All data were anonymised prior to analysis, and patient confidentiality was strictly maintained.

3. Results

3.1. Demographic and Clinical Characteristics

A total of 89 patients with systemic lupus erythematosus (SLE) were included in the analysis. The demographic and clinical characteristics of the study population are summarized in Table 1. The mean age of the patients was 38.85 ± 13.35 years, with a mean age at diagnosis of 30.56 ± 13.05 years. The mean disease duration was 9.09 ± 8.00 years.

Most patients were female (94.4%, n = 84) and of Malay ethnicity (86.5%, n = 77). High-dose prednisolone exposure (>1 mg/kg/day) was documented in 64.0% of patients (n = 57). Hypertension was present in 33.7% (n = 30), while diabetes mellitus was observed in 11.2% (n = 10). The mean number of disease relapses was 0.90 ± 1.10.

All patients (100%) received hydroxychloroquine during the disease course. Azathioprine and cyclophosphamide were used in 62.9% (n = 56) and 29.2% (n = 26) of patients, respectively. High antinuclear antibody (ANA) titres were detected in 91.0% of patients (n = 81), and anti–double-stranded DNA antibodies were positive in 68.5% (n = 61). The mean cumulative complement levels were 1.04 ± 0.34 for C3 and 0.20 ± 0.10 for C4. Lupus anticoagulant and anti-cardiolipin antibodies were present in 11.2% (n = 10) and 6.7% (n = 6) of patients, respectively.

Variable	Mean (SD)	n (%)
Age	38.85 (13.35)	
Age at diagnosis	30.56 (13.05)	
Disease duration (years)	9.09 (8.00)	

Female		84 (94.4)
Male		5 (5.6)
Malay		77 (86.5)
Chinese		10 (11.2)
Indian		1 (1.1)
Others		1 (1.1)
Hypertension		30 (33.7)
Diabetes mellitus		10 (11.2)
Hydroxychloroquine use		89 (100)

Table 1: Demographic Data of SLE Patients Involved in this Study (n=89)

3.2. Disease Damage among SLE Patients

The distribution of organ damage according to the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) among the 89 patients is summarised in Table 2. No organ damage (SDI ≥ 1) was observed in the gastrointestinal, musculoskeletal, or cutaneous domains.

Ocular damage was the most frequently affected organ system, occurring in 11 patients (12.4%). Neuropsychiatric and cardiovascular damage were uncommon; each observed in 2 patients (2.2%). Pulmonary involvement was infrequent, with pulmonary hypertension reported in 3.4% of patients, pulmonary fibrosis in 2.2%, and pulmonary infarction in 1.1%.

Peripheral vascular damage and premature gonadal failure were each documented in 1.1% of patients. Endocrine damage related to diabetes mellitus was observed in 7 patients (7.9%), while malignancy-related organ damage was reported in 2 patients (2.2%).

Organ system	No damage n (%)	Damage n (%)
Ocular	78 (87.6)	11 (12.4)
Neuropsychiatric	87 (97.8)	2 (2.2)
Pulmonary hypertension	86 (96.6)	3 (3.4)
Pulmonary fibrosis	87 (97.8)	2 (2.2)
Pulmonary infarction	88 (98.9)	1 (1.1)
Cardiovascular	87 (97.8)	2 (2.2)
Peripheral vascular	88 (98.9)	1 (1.1)
Diabetes-related damage	82 (92.1)	7 (7.9)
Malignancy	87 (97.8)	2 (2.2)

Table 2: Distribution of Organ Damage of sle Patients (SDI domains)

3.3. Association of SDI Score with Clinico-Demographic Features

Table 3 summarises the baseline characteristics of 89 patients with systemic lupus erythematosus stratified by the presence of organ damage (SDI ≥1). Patients with organ damage were older (mean age 41.83 ± 14.25 years vs. 36.19 ± 12.03 years) and had a longer disease duration (11.09 ± 9.19 vs. 7.31 ± 6.35 years) compared to those without damage. A higher relapse rate was also observed in the organ damage group.

Hypertension was more prevalent among patients with organ damage (50.0% vs. 19.1%). Similarly, a greater proportion had a history of high-dose prednisolone exposure (>1 mg/kg/day) (71.4% vs. 57.4%). Use of immunosuppressive therapy was more frequent in the organ damage group, particularly azathioprine (73.8%) and cyclophosphamide (45.2%). Hydroxychloroquine was prescribed universally across both groups.

Regarding serological markers, high antinuclear antibody titres (>1:160) were common in both groups but slightly less frequent among patients with organ damage (85.7% vs. 95.7%). The prevalence of anti–double-stranded DNA antibodies was comparable between groups (69.0% vs. 68.1%). Complement levels were similar, with mean C3 levels of 1.02 ± 0.35 vs. 1.05 ± 0.33 and C4 levels of 0.19 ± 0.10 vs. 0.20 ± 0.11 in patients with and without organ damage, respectively.

Notably, lupus anticoagulant positivity was higher among patients with organ damage (19.0% vs. 4.3%), and anti-cardiolipin antibodies were detected only in the organ damage group (14.3%).

Variable	No damage	Damage
Age (years)	36.19 (12.03)	41.83 (14.25)
Disease duration	7.31 (6.35)	11.09 (9.19)
Hypertension	9 (19.1)	21 (50.0)
Diabetes mellitus	1 (2.1)	9 (21.4)
Cyclophosphamide use	7 (14.9)	19 (45.2)

Table 3: Comparison between Patients with and without Organ Damage

As shown in Table 4, univariable logistic regression identified several factors significantly associated with organ damage, including older age, longer disease duration, hypertension, diabetes mellitus, azathioprine use, cyclophosphamide exposure, and lupus anticoagulant positivity.

Variables with $p < 0.25$ and those of clinical relevance were entered into the multivariable logistic regression model. After adjustment, only diabetes mellitus and cyclophosphamide exposure remained independently associated with organ damage. (Table 5).

Variable	Crude OR	95% CI	p-value
Age	1.034	1.000–1.068	0.049
Disease duration	1.065	1.006–1.127	0.030
Hypertension	4.222	1.640–10.867	0.003
Diabetes mellitus	12.545	1.515–103.873	0.019
Cyclophosphamide	4.720	1.724–12.922	0.003

Table 4: Association of Continuous Variables with SDI score. p < .05 is Emboldened

Variable	Adjusted OR	95% CI	p-value
Diabetes mellitus	15.305	1.770–132.323	0.013
Cyclophosphamide	5.370	1.885–15.301	0.002

Table 5: Parameters Associated with SDI according to Multivariable Logistic Regression Analysis

4. Discussion

This retrospective cohort study highlights a substantial burden of irreversible organ damage among our patients with systemic lupus erythematosus (SLE), with 47.2% of patients demonstrating damage (SDI ≥1). This prevalence is highly consistent with prior regional and national Malaysian cohorts and aligns with global estimates, where approximately one-third to one-half of patients develop permanent damage within the first five years of disease [5,6]. These findings reinforce that, despite improvements in survival, long-term morbidity remains a persistent and universal challenge in SLE.

The pattern of organ involvement in this cohort reveals both concordance and divergence with existing literature [7,8]. Ocular damage, primarily cataracts, emerged as the most frequent manifestation, likely reflecting cumulative glucocorticoid exposure. This is consistent with international data linking corticosteroid burden to early damage accrual [9]. Diabetes-related damage was the second most common domain, emphasizing the role of treatment-related metabolic complications. In contrast, the absence of gastrointestinal, musculoskeletal, and cutaneous damage differs from several international cohorts, where these domains are more prominent [10,11]. This discrepancy may reflect variations in local management practices, earlier steroid tapering, or population-specific genetic factors.

Multivariable analysis identified diabetes mellitus and prior cyclophosphamide exposure as independent predictors of organ damage. The strong association with diabetes underscores its dual role as both a comorbidity and a contributor to cumulative damage. Cyclophosphamide exposure likely reflects more severe disease phenotypes, such as lupus nephritis or neuropsychiatric SLE, in addition to its known treatment-related toxicities [12,13]. These findings are consistent with global evidence and highlight the need for careful risk stratification and consideration of less toxic therapeutic alternatives.

Univariable analysis further identified older age, longer disease duration, hypertension, and lupus anticoagulant positivity as significant factors associated with damage. These results support the concept of cumulative damage accrual over time and emphasize the contribution of cardiovascular risk factors and prothrombotic

states [14,15]. Notably, while antinuclear antibodies were highly prevalent, they were not predictive of damage, underscoring the greater prognostic value of specific autoantibody profiles.

From a therapeutic perspective, universal hydroxychloroquine use represents a key strength in this cohort, consistent with its established protective role in reducing disease activity, damage accrual, and mortality [16,17]. However, the high prevalence of corticosteroid exposure remains concerning, particularly given its association with cataracts and diabetes. These findings highlight the urgent need for steroid-sparing strategies and optimized long-term disease control.

Several limitations should be acknowledged. The single-centre, retrospective design limits generalizability and introduces potential documentation bias. The modest sample size may have reduced statistical power, particularly for less common damage domains, and contributed to unstable regression estimates in sparse data categories. These findings should therefore be interpreted cautiously and validated in larger, prospective studies.

5. Conclusion

In conclusion, nearly half of our patients with SLE experience irreversible organ damage, with ocular and metabolic complications predominating. Diabetes mellitus and cyclophosphamide exposure are key predictors of damage, underscoring the importance of comprehensive risk factor management and careful therapeutic selection. Despite optimal hydroxychloroquine use, the burden of corticosteroid-related toxicity remains significant, highlighting the need for steroid-sparing approaches and treat-to-target strategies. Future prospective, multicentre studies are warranted to better define longitudinal damage trajectories and optimize long-term outcomes in Malaysian patients with SLE.

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Author Contributions

MSMF., WSWG., contributed to the study conception and design. Material preparation, data collection and analysis were performed by MSMF. The first draft of the manuscript was written by MSMF. WSWG, SNMN, HS, NDMY read and approved the final manuscript.

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Data Availability

The data presented in the study are available on request from the corresponding author on reasonable request following permission by the ethics committee of the hospital.

Declarations Ethical Approval

The procedures used in this study adhere to the tenets of the Declaration of Helsinki. This study was approved by the Research Ethics Committee USM hospital (20th March 2023, approval number 66039). Informed consent Inform consent was waived for this retrospective study. The study was approved by the Ethics Committee hospital, and all participant data was handled with strict confidentiality.

Consent for Publication

Not applicable.

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