RESEARCH PAPER

Disease Activity and Disease Duration as Independent Predictors of Mortality in Patients with Systemic Lupus Erythematosus

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ABSTRACT

Background and aim: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by recurrent flares and progressive organ damage, resulting in substantial morbidity and mortality. Although numerous clinical factors have been associated with mortality, the independent contribution of disease activity and disease duration remains uncertain. This study aimed to identify independent predictors of in-hospital mortality among hospitalized patients with SLE.

Methods: This retrospective observational study was conducted at Dr. Wahidin Sudirohusodo Hospital, a tertiary referral center in Makassar, Indonesia. A total of 328 hospitalized adult patients with SLE admitted between January 2020 and December 2025 were initially identified from the hospital medical record database. After applying the predefined inclusion and exclusion criteria and excluding patients with incomplete clinical data, 123 patients were included in the final analysis, comprising 51 non-survivors and 72 survivors. Demographic characteristics, disease duration, flare episodes, disease activity assessed using the Mexican Systemic Lupus Erythematosus Disease Activity Index (Mex-SLEDAI), cardiovascular disease, hypertension, type 2 diabetes mellitus, infection, chronic kidney disease, cerebrovascular disease, and the number of comorbidities were extracted from medical records. Univariable and multivariable logistic regression analyses using the backward likelihood ratio method were performed to identify independent predictors of in-hospital mortality, with results reported as odds ratios (ORs) and 95% confidence intervals (CIs)..

Results: Of the 123 hospitalized patients with SLE, 51 (41.5%) died during hospitalization. Univariable analysis showed that flare episodes, severe disease activity, disease duration ≥1-year, cardiovascular disease, hypertension, infection, chronic kidney disease, cerebrovascular disease, and ≥3 comorbidities were significantly associated with mortality (all $P < 0.05$). In the final multivariable model, severe disease activity (adjusted OR 43.80, 95% CI 13.05–146.94; $P = 0.001$) and disease duration ≥1 year (adjusted OR 4.73, 95% CI 1.34–16.67; $P = 0.016$) remained independent predictors of in-hospital mortality.

Conclusions: Severe disease activity and prolonged disease duration were identified as the strongest independent predictors of in-hospital mortality among hospitalized patients with SLE. Routine assessment of disease activity using the Mex-SLEDAI, together with early identification of patients with prolonged disease duration, may improve risk stratification and support timely therapeutic interventions to reduce mortality.

Keywords: Systemic lupus erythematosus; Disease activity; Mex-SLEDAI; hospital mortality;

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease characterized by relapsing–remitting inflammation and heterogeneous clinical manifestations ranging from mild mucocutaneous involvement to life-threatening multiorgan dysfunction. Despite substantial advances in diagnosis and immunosuppressive therapy, patients with SLE continue to experience significantly higher mortality than the general population. The risk of death has been reported to be

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approximately threefold higher during the first decade after diagnosis, with 10-year and 20-year survival rates of approximately 85% and 75%, respectively. Mortality patterns differ across populations and stages of disease; disease activity, severe infections, and lupus nephritis remain the predominant causes of death in developing countries, whereas cardiovascular disease and malignancy account for a greater proportion of late mortality in developed countries. These findings highlight that mortality in SLE is influenced not only by disease-related factors but also by demographic characteristics, comorbidities, and healthcare settings.[1–3]

Numerous studies have identified predictors associated with poor survival in SLE, including older age at onset, male sex, persistent high disease activity, recurrent flares, lupus nephritis, chronic kidney disease, cardiovascular complications, infections, hypertension, diabetes mellitus, hematological abnormalities, antiphospholipid antibodies, elevated inflammatory markers, and the cumulative burden of comorbidities. Persistent disease activity contributes to irreversible organ damage and increases exposure to high-dose glucocorticoids and immunosuppressive agents, thereby further increasing the risks of infection, cardiovascular events, and mortality. Conversely, achieving remission or a lupus low disease activity state (LLDAS) has consistently been associated with improved long-term survival. Although these risk factors have been extensively investigated, their relative contribution to mortality varies among different populations because of differences in ethnicity, socioeconomic conditions, disease characteristics, and access to healthcare.[4,5]

Given the multifactorial nature of mortality in SLE, identifying independent prognostic factors within local populations is essential for improving risk stratification and optimizing clinical management. Evidence from Indonesia remains limited, particularly regarding the combined impact of disease activity and disease duration on survival outcomes. Therefore, this study aimed to identify independent predictors of mortality among patients with systemic lupus erythematosus, with a particular focus on disease activity and disease duration. The findings are expected to provide evidence to support early risk assessment, individualized management strategies, and improved long-term outcomes for patients with SLE.

METHODS AND MATERIALS

Study design and subjects

This retrospective observational analytical study was conducted to identify independent predictors of in-hospital mortality among patients with SLE. The study was performed at Dr. Wahidin Sudirohusodo Hospital, a tertiary referral hospital in Makassar, Indonesia. Medical records of hospitalized adult patients with SLE admitted between January 2020 and December 2025 were retrospectively reviewed, while data collection was conducted from December 2025 to March 2026.

Initially, 328 hospitalized patients with a diagnosis of SLE were identified through the hospital medical record database. Among these, 92 patients died during hospitalization and 236 survived. After applying the predefined inclusion and exclusion criteria and excluding patients with incomplete clinical data, 123 patients were eligible for the final analysis, comprising 51 non-survivors and 72 survivors (Figure 1). Patients aged ≥18 years with a confirmed diagnosis of SLE according to the 1997 American College of Rheumatology (ACR), 2012 Systemic Lupus International Collaborating Clinics (SLICC), or 2019 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria were included. Patients with incomplete medical records or missing information on mortality status and key study variables were excluded.

Adult patients (≥18 years) diagnosed with SLE according to the 1997 American College of Rheumatology (ACR) classification criteria, the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria, or the 2019 European Alliance of Associations for Rheumatology/American College of Rheumatology (EULAR/ACR) classification criteria were eligible for inclusion. Patients were identified using the International Classification of Diseases, Tenth Revision (ICD-10) code M32. Patients were included if complete medical records were available, including demographic characteristics, disease duration, disease activity, immunological profile (antinuclear antibody [ANA] and complement C3), treatment history, comorbidities, and mortality status. Patients with incomplete medical records, concomitant connective tissue diseases without fulfilling the SLE classification criteria, or missing outcome data were excluded..

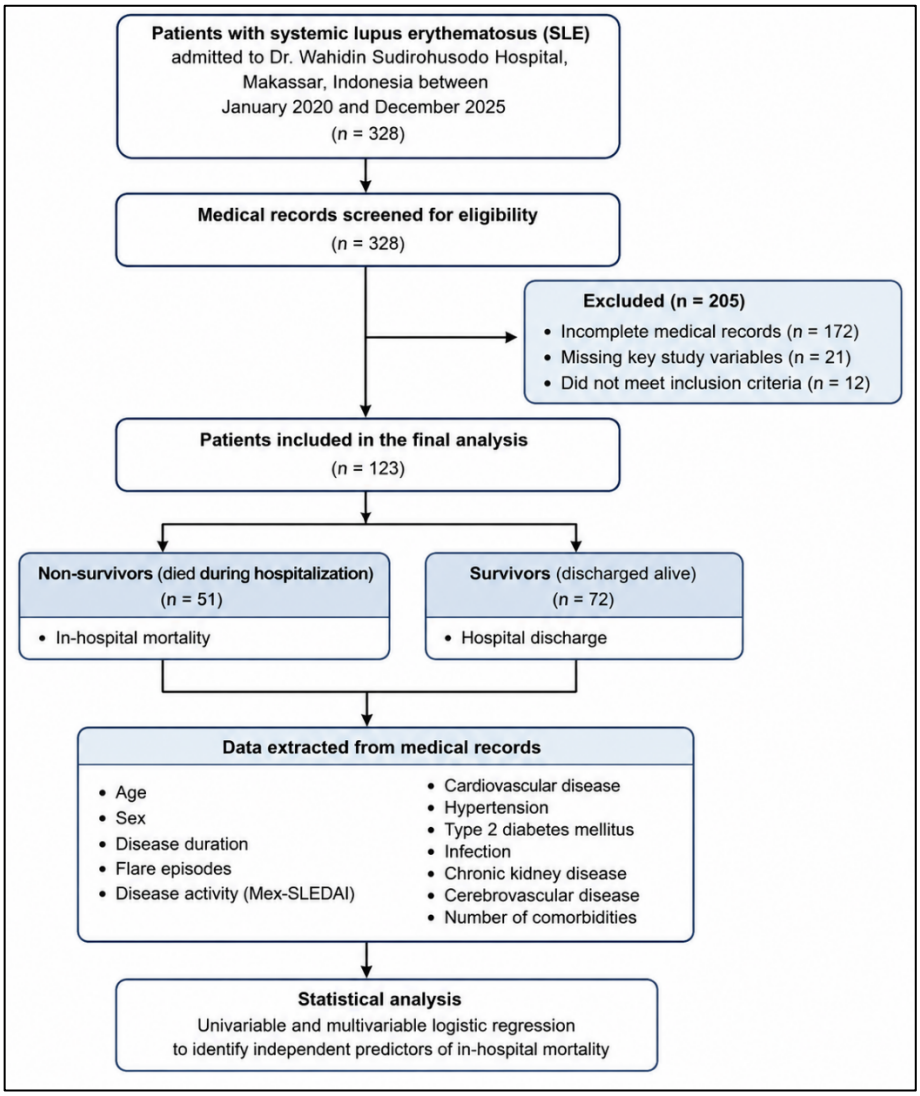

Figure 1. Flow diagram of patient selection and study enrollment. A total of 328 hospitalized patients with systemic lupus erythematosus were identified from the hospital medical record database between January 2020 and December 2025. After applying the predefined eligibility criteria and excluding patients with incomplete medical records, 123 patients were included in the final analysis, comprising 51 non-survivors and 72 survivors.

Ethical approval and informed consent

This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Hasanuddin University and Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia (Approval No. 1188/UN4.6.4.5.31/PP36/2025, approved on 24 December 2025). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. The requirement for written informed consent was waived by the Health Research Ethics Committee because of the retrospective nature of the study and the use of anonymized medical records.

Data collection

Demographic, clinical, immunological, and outcome data were retrospectively extracted from the electronic medical records of hospitalized patients with SLE. Baseline demographic characteristics included age and sex. Clinical variables comprised disease duration, disease activity, flare episodes, hypertension, diabetes mellitus, cardiovascular disease, chronic kidney disease, cerebrovascular disease, infections, malignancy, and the number of comorbidities. Immunological variables included antinuclear antibody (ANA) and complement C3 results. Information regarding treatment history, including immunosuppressive therapy, glucocorticoid use, and pulse methylprednisolone administration, was also collected. The primary outcome was all-cause in-hospital mortality.

SLE diagnosis was established according to the 1997 ACR classification criteria, the 2012 SLICC classification criteria, or the 2019 EULAR/ACR classification criteria. Patients were identified using the International Classification of Diseases, Tenth Revision (ICD-10) code M32. Disease duration was defined as the interval between the date of SLE diagnosis and the date of hospitalization. Disease activity was assessed using the Mex-SLEDAI, a validated instrument for evaluating SLE disease activity

without requiring immunological parameters. Although the Mex-SLEDAI classifies disease activity into inactive (0–1), mild (2–5), moderate (6–9), high (10–13), and very high (≥14) categories, for the purpose of this study, patients were categorized into two groups only: moderate disease activity (Mex-SLEDAI score 6–9) and severe disease activity (Mex-SLEDAI score ≥10, including high and very high activity). This categorization was adopted to facilitate statistical analysis and because hospitalized patients in this cohort predominantly presented with moderate-to-severe disease activity. Flare episodes were defined as documented worsening of disease activity requiring escalation of treatment within the previous 12 months.

Comorbidities were defined according to documented physician diagnoses in the medical records. Cardiovascular disease included ischemic heart disease, heart failure, arrhythmia, or other clinically diagnosed cardiovascular disorders. Chronic kidney disease was defined according to the kidney disease: Improving Global Outcomes (KDIGO) criteria or a documented history of chronic kidney disease. Infection was defined as clinically or microbiologically confirmed bacterial, viral, fungal, or parasitic infection requiring antimicrobial therapy during hospitalization. Malignancy was defined as any documented solid or hematologic malignancy before or during the study period. The number of comorbidities was calculated as the total number of coexisting chronic medical conditions documented for each patient.

All data were extracted using a standardized data collection form by trained investigators. To ensure data accuracy and completeness, medical records were independently reviewed and cross-checked prior to analysis. Patients with incomplete information regarding the primary outcome or key study variables were excluded from the final analysis.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Kolmogorov–Smirnov test. Normally distributed data are presented as mean ± standard deviation (SD), whereas non-normally distributed data are presented as median and interquartile range (IQR). Categorical variables are expressed as frequencies and percentages.

Baseline characteristics between survivors and non-survivors were compared using the independent-samples t-test or Mann–Whitney U test for continuous variables, as appropriate, and the chi-square test or Fisher's exact test for categorical variables.

To identify factors associated with in-hospital mortality, univariable logistic regression analysis was initially performed for each independent variable. Variables evaluated included age, sex, disease duration, disease activity, flare episodes, hypertension, diabetes mellitus, cardiovascular disease, chronic kidney disease, cerebrovascular disease, infections, malignancy, and the number of comorbidities. Crude odds ratios (ORs) and their corresponding 95% confidence intervals (95% CIs) were calculated.

Variables with a P-value <0.25 in the univariable analysis and variables considered clinically relevant based on previous evidence were subsequently entered into a multivariable logistic regression model using the backward likelihood ratio method to identify independent predictors of mortality. Because the primary objective of this study was to evaluate whether disease activity and disease duration independently predicted mortality, these two variables were retained during model development irrespective of intermediate selection procedures. Adjusted odds ratios (aORs) with 95% confidence intervals (95% CIs) were reported for the final model.

Model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test, and multicollinearity among independent variables was assessed using the variance inflation factor (VIF) before multivariable analysis. Statistical significance was defined as a two-sided P-value <0.05.

RESULT

Baseline Characteristics of the Study

A total of 123 hospitalized patients with systemic lupus erythematosus (SLE) were included in the study, comprising 51 non-survivors and 72 survivors. Compared with survivors, non-survivors more frequently had ≥2 flare episodes (60.8% vs. 29.3%), severe disease activity (83.3% vs. 8.7%), disease duration ≥1 year (53.9% vs. 21.3%), cardiovascular disease (68.6% vs. 41.0%), infection (56.9% vs. 17.0%), chronic kidney disease (57.1% vs. 15.2%), cerebrovascular disease (100% vs. 59.7%), and ≥3 comorbidities (73.5% vs. 20.3%). Baseline demographic and clinical characteristics of the study population are summarized in Table 1.

Table 1. Baseline Characteristics of the Study

Variable	Category	Non-survivors (n = 51)	Survivors (n = 72)	Overall (n = 123)
Sex	Female	51 (41.5)	72 (58.5)	123 (100.0)
	Male	0 (0.0)	0 (0.0)	0 (0.0)
Age (years)	<30	28 (46.7)	32 (53.3)	60 (48.8)
	≥30	23 (36.5)	40 (63.5)	63 (51.2)
Flare episodes	<2 episodes	22 (29.3)	53 (70.7)	75 (61.0)

	≥2 episodes	29 (60.4)	19 (39.6)	48 (39.0)
Disease activity (Mex-SLEDAI)	Moderate	6 (8.7)	63 (91.3)	69 (56.1)
	Severe	45 (83.3)	9 (16.7)	54 (43.9)
Disease duration	<1 year	10 (21.3)	37 (78.7)	47 (38.2)
	≥1 year	41 (53.9)	35 (46.1)	76 (61.8)
Cardiovascular disease	No	18 (24.0)	57 (76.0)	75 (61.0)
	Yes	33 (68.8)	15 (31.3)	48 (39.0)
Type 2 diabetes mellitus	No	50 (41.0)	72 (59.0)	122 (99.2)
	Yes	1 (100.0)	0 (0.0)	1 (0.8)
Hypertension	No	29 (34.9)	54 (65.1)	83 (67.5)
	Yes	22 (55.0)	18 (45.0)	40 (32.5)
Infection	No	8 (17.0)	39 (83.0)	47 (38.2)
	Yes	43 (56.6)	33 (43.4)	76 (61.8)
Chronic kidney disease	No	7 (15.2)	39 (84.8)	46 (37.4)
	Yes	44 (57.1)	33 (42.9)	77 (62.6)
Cerebrovascular disease	No	46 (39.0)	72 (61.0)	118 (95.9)
	Yes	5 (100.0)	0 (0.0)	5 (4.1)
Number of comorbidities	<3	15 (20.3)	59 (79.7)	74 (60.2)
	≥3	36 (73.5)	13 (26.5)	49 (39.8)
Data are presented as n (%). Disease activity was assessed using the Mexican Systemic Lupus Erythematosus Disease Activity Index (Mex-SLEDAI) and categorized as moderate (score 6–9) or severe (score ≥10).				

Univariable Analysis of Mortality-Associated Factors in Patients with Systemic Lupus Erythematosus

Univariable logistic regression analysis showed that flare episodes, disease activity, disease duration, cardiovascular disease, hypertension, infection, chronic kidney disease, cerebrovascular disease, and the number of comorbidities were significantly associated with in-hospital mortality (all $P < 0.05$). In contrast, age, sex, and type 2 diabetes mellitus were not significantly associated with mortality ($P > 0.05$). No patients with malignancy were identified during the study period; therefore, this variable was not included in the regression analysis (Table 2).

Table 2. Univariable Analysis of Factors Associated with Mortality

Variable	Non-survivors n (%)	Survivors n (%)	Crude OR (95% CI)	P value
Age ≥30 years	23 (36.5)	40 (63.5)	1.522 (0.740–3.130)	0.253
Flare episodes ≥2	29 (60.4)	19 (39.6)	3.677 (1.715–7.884)	0.001
Severe disease activity	45 (83.3)	9 (16.7)	52.500 (17.449–157.963)	<0.001
Disease duration ≥1 year	41 (53.9)	35 (46.1)	4.334 (1.887–9.995)	<0.001
Cardiovascular disease	33 (68.8)	15 (31.3)	6.697 (3.105–15.633)	<0.001
Type 2 diabetes mellitus	1 (100.0)	0 (0.0)	2.440 (1.972–3.091)	0.233
Hypertension	22 (55.0)	18 (45.0)	2.276 (1.055–4.911)	0.034
Infection	43 (56.6)	33 (43.4)	6.352 (2.620–15.402)	<0.001
Chronic kidney disease	44 (57.1)	33 (42.9)	7.429 (2.953–18.687)	<0.001
Cerebrovascular disease	5 (100.0)	0 (0.0)	2.565 (2.047–3.215)	0.007
≥3 comorbidities	36 (73.5)	13 (26.5)	10.892 (4.653–25.498)	<0.001
Data are presented as n (%). Crude odds ratios (ORs) with 95% confidence intervals (CIs) were estimated using univariable logistic regression.				

Multivariable Logistic Regression Analysis of Factors Associated with Mortality

Multivariable logistic regression analysis identified disease activity and disease duration as independent predictors of in-hospital mortality in patients with systemic lupus erythematosus (Table 3). Patients with severe disease activity had a significantly higher risk of mortality than those with moderate disease activity

(adjusted OR, 43.80; 95% CI, 13.05–146.94; P = 0.001). Likewise, patients with a disease duration ≥1 year had a 4.72-fold higher risk of mortality than those with a disease duration <1 year (adjusted OR, 4.72; 95% CI, 1.31–17.17; P = 0.017). None of the remaining covariates, including cardiovascular disease, hypertension, infection, chronic kidney disease, or the number of comorbidities, remained independently associated with mortality after adjustment.

Table 3. Multivariable Logistic Regression Analysis of Factors Associated with In-Hospital Mortality

Variable	Adjusted OR (95% CI)	P value
Severe disease activity	43.80 (13.05–146.94)	0.001
Disease duration ≥1 year	4.73 (1.34–16.67)	0.016
Variables entered into the multivariable model included disease activity, disease duration, cardiovascular disease, hypertension, infection, chronic kidney disease, and number of comorbidities. The final model retained disease activity and disease duration as independent predictors of mortality.		

DISCUSSION

The present study identified disease activity and disease duration as independent predictors of in-hospital mortality among patients with systemic lupus erythematosus (SLE) after adjustment for multiple clinically relevant confounding factors. In the univariable analysis, several variables, including flare episodes, cardiovascular disease, hypertension, infection, chronic kidney disease, cerebrovascular disease, and the number of comorbidities, were significantly associated with mortality. However, following multivariable logistic regression analysis using the backward likelihood ratio method, only severe disease activity and disease duration of ≥1 year remained independently associated with an increased risk of death. Patients with severe disease activity had an approximately 44-fold higher risk of in-hospital mortality, whereas those with a disease duration of at least one year had an approximately 4.7-fold higher risk of death compared with their respective reference groups.

These findings suggest that persistent inflammatory activity and cumulative disease burden are the principal determinants of mortality among hospitalized patients with SLE. Although several comorbid conditions were associated with an increased risk of death in the univariable analysis, their effects appeared to be largely mediated by disease activity and disease duration. In other words, high disease activity not only reflects uncontrolled systemic inflammation but is also associated with progressive organ damage, the need for more intensive immunosuppressive therapy, an increased susceptibility to severe infections, and multiorgan complications that ultimately contribute to mortality. These findings are consistent with the current concept that controlling disease activity is the primary therapeutic goal in the management of SLE. This strategy is emphasized in the 2023 EULAR recommendations, which advocate sustained remission and LLDAS as key treatment targets to minimize irreversible organ damage and improve long-term survival.[6]

The present study identified severe disease activity as the strongest independent predictor of in-hospital mortality among patients with SLE. After adjustment for multiple clinically relevant confounding factors, patients with severe disease activity had an approximately 44-fold higher risk of death than those with moderate disease activity. The magnitude of this adjusted odds ratio highlights disease activity as the principal determinant of short-term clinical outcomes in hospitalized patients with SLE. These findings are consistent with previous cohort studies demonstrating that high disease activity is a major determinant of organ damage, the need for intensive immunosuppressive therapy, and mortality in patients with SLE.[5,7]

From a biological perspective, the association between disease activity and mortality can be explained by several underlying pathophysiological mechanisms. High disease activity reflects persistent immune dysregulation characterized by autoreactive B- and T-cell activation, excessive autoantibody production, immune complex deposition, complement activation, and increased production of pro-inflammatory cytokines, including type I interferons, interleukin-6, and tumor necrosis factor-α. Sustained systemic inflammation promotes endothelial dysfunction, increased vascular permeability, microvascular thrombosis, and progressive tissue injury involving multiple organ systems, particularly the kidneys, central nervous system, lungs, and cardiovascular system. Collectively, these pathological processes increase the risk of irreversible organ failure and multiorgan dysfunction, which remain the leading causes of death among patients with active SLE.[8]

In addition to causing direct organ injury, severe disease activity also increases the risk of treatment-related complications. Patients with highly active disease frequently require aggressive immunosuppressive therapy, including high-dose glucocorticoids, intravenous methylprednisolone pulse therapy, cyclophosphamide, mycophenolate mofetil, or rituximab. Although these therapeutic strategies are effective in controlling inflammation, prolonged or intensive immunosuppression substantially increases susceptibility to opportunistic infections, sepsis, and hospital-acquired infections. Therefore, mortality in patients with severe SLE is likely the consequence of a complex interaction between uncontrolled systemic inflammation and complications associated with immunosuppressive treatment.[6]

Our findings further support the current treat-to-target strategy in SLE, which emphasizes the achievement of remission or LLDAS as the primary therapeutic goal. Prospective studies conducted by the Asia-Pacific Lupus

Collaboration have consistently demonstrated that patients who maintain LLDAS for a substantial proportion of follow-up experience significantly lower risks of organ damage accrual and mortality than those with persistently active disease. Likewise, sustained remission has been associated with fewer disease flares, reduced glucocorticoid exposure, and improved long-term clinical outcomes. These observations reinforce the concept that effective control of disease activity not only alleviates clinical manifestations but also represents the most important strategy for improving survival in patients with SLE.[9]

The present findings are also consistent with those reported by Ocampo-Piraquive et al. (2018), who demonstrated that high disease activity contributes to mortality both directly and indirectly through accelerated organ damage. Similarly, Pattanaik et al. (2020) identified disease activity as one of the strongest predictors of mortality across multiple international SLE cohorts. Although the effect size observed in the present study was greater than that reported in previous studies, this difference is likely attributable to the characteristics of the study population. All participants in the present study were hospitalized at a tertiary referral center, where patients generally presented with more severe disease manifestations, multiorgan involvement, or acute life-threatening complications requiring intensive medical management. Consequently, the distribution of disease severity in our cohort was substantially greater than that observed in community-based or outpatient populations included in most epidemiological studies.[5,7]

The substantially higher adjusted odds ratio observed in the present study compared with previous reports should be interpreted in the context of the study population and study design. First, this study exclusively included hospitalized patients from a tertiary referral center, where severe disease manifestations, multiorgan involvement, and acute complications are more prevalent than in community-based or outpatient cohorts. Second, disease activity was categorized into only two clinically relevant categories (moderate and severe) using the Mex-SLEDAI, reflecting the characteristics of hospitalized patients with active SLE. The absence of patients with mild disease or remission likely increased the contrast between exposure groups and may have contributed to the larger estimated effect size. Finally, the relatively modest sample size and the limited number of mortality events may have resulted in wider confidence intervals and less precise estimates. Therefore, although the magnitude of the adjusted odds ratio should be interpreted with caution, the observed association is biologically plausible and remains consistent with previous studies identifying uncontrolled disease activity as a major determinant of mortality in SLE.

From a clinical perspective, these findings underscore the importance of routinely assessing disease activity using validated instruments such as the Mex-SLEDAI in hospitalized patients with SLE. Early identification of patients with severe disease activity enables prompt risk stratification, closer clinical monitoring, timely optimization of immunosuppressive therapy, and implementation of preventive strategies to reduce life-threatening complications. Therefore, disease activity should be regarded not only as an indicator of current clinical status but also as a robust prognostic marker for predicting both short-term and long-term outcomes in patients with systemic lupus erythematosus.

The present study identified disease duration of ≥1 year as an independent predictor of in-hospital mortality among patients with systemic lupus erythematosus (SLE), with an approximately 4.7-fold increased risk of death compared with patients whose disease duration was less than one year. This finding suggests that prolonged disease duration reflects an increasing cumulative burden of disease and progressive organ damage, both of which contribute substantially to adverse clinical outcomes. Although advances in immunosuppressive therapy and multidisciplinary management have significantly improved long-term survival in patients with SLE, persistent immune dysregulation and chronic inflammation continue to promote irreversible tissue injury, thereby increasing the risk of morbidity and mortality over time. These findings support the concept that mortality in SLE is determined not only by current disease activity but also by the cumulative effects of prolonged disease exposure and organ damage accumulation.[6,8]

Several mechanisms may explain the association between longer disease duration and increased mortality. Chronic immune activation promotes sustained autoantibody production, complement activation, endothelial dysfunction, and persistent inflammatory injury involving multiple organs. Recurrent disease flares further accelerate irreversible organ damage, particularly affecting the kidneys, cardiovascular system, lungs, central nervous system, and hematological system. In addition, prolonged exposure to glucocorticoids and immunosuppressive agents contributes to treatment-related complications, including hypertension, diabetes mellitus, dyslipidemia, osteoporosis, opportunistic infections, and accelerated atherosclerosis. Consequently, longer disease duration represents not only the length of time since diagnosis but also cumulative exposure to chronic inflammation and treatment-related toxicity, both of which adversely influence patient survival.

Our findings are consistent with previous longitudinal studies demonstrating that cumulative organ damage is one of the strongest determinants of mortality in SLE. Ocampo-Piraquive et al. reported that increasing SLICC/ACR-DI scores were independently associated with reduced survival. Similarly, Pattanaik et al. concluded in their systematic review that prolonged disease duration contributes to mortality primarily through irreversible organ damage, particularly lupus nephritis, cardiovascular complications, and severe infections. Although organ damage was not directly quantified in the present study, the persistence of disease duration as an independent predictor after adjustment for multiple clinical variables

suggests that disease duration may serve as a surrogate marker for cumulative disease burden and irreversible organ injury.

From a clinical perspective, these findings emphasize that long-term management of SLE should extend beyond achieving remission or low disease activity. Patients with longer disease duration require continuous surveillance for chronic organ damage and treatment-related complications, even when disease activity appears to be adequately controlled. Therefore, strategies aimed at minimizing cumulative glucocorticoid exposure, preventing recurrent disease flares, and routinely monitoring renal and cardiovascular function are essential to improve long-term survival in patients with SLE.

Despite these limitations, this study has several important strengths. To our knowledge, this is one of the first studies from Indonesia to identify disease activity and disease duration as independent predictors of in-hospital mortality among patients with systemic lupus erythematosus (SLE). By simultaneously evaluating multiple clinically relevant variables using multivariable logistic regression, this study was able to adjust for potential confounding factors and provide real-world evidence from a tertiary referral hospital that manages patients with moderate-to-severe SLE.

Nevertheless, several limitations should be acknowledged. The retrospective, single-center design may have introduced information bias, residual confounding, and limited the generalizability of the findings. In addition, the relatively modest sample size and the absence of several important prognostic variables, including cumulative glucocorticoid exposure, treatment adherence, SLICC/ACR Damage Index, antiphospholipid antibody profile, and anti-double-stranded DNA antibody levels, may have influenced the results. Furthermore, because the primary outcome was restricted to in-hospital mortality, long-term survival and post-discharge outcomes could not be evaluated. Therefore, prospective multicenter studies with larger sample sizes and longer follow-up are needed to validate these findings and further clarify the impact of cumulative organ damage and treatment-related factors on mortality in patients with SLE.

CONCLUSION

Among hospitalized patients with systemic lupus erythematosus, severe disease activity and prolonged disease duration emerged as the strongest independent predictors of in-hospital mortality. These findings highlight that persistent systemic inflammation and cumulative disease burden, rather than individual comorbid conditions, are the principal determinants of short-term survival in this population. Routine assessment of disease activity using the Mex-SLEDAI and early identification of patients with prolonged disease duration may improve risk stratification and guide timely therapeutic interventions. Further multicenter prospective studies are needed to validate these findings and refine mortality prediction models for patients with SLE.

Ethic approval:
This study has been approved by the Research Ethics Committee of the Faculty of Medicine, Hasanuddin University, through the issuance of an ethics approval letter Number: 1188/UN4.6.4.5.31/PP36/2025, approval date 24 December 2025. This study complies with ethical principles, ensuring the protection of participants' rights and confidentiality.

Conflict of Interest:
The authors declare no conflict of interest.

Authors Contribution:
FJ, FS, and HR drafted the manuscript. FJ, FS, HR, and AS designed and concepted the study. FJ and FS collected and analyzed and interpreted the data. HR, SB, and RHM revised manuscript critically for important intellectual content. All authors participated in the final draft preparation, manuscript revision, and critical evaluation of the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work

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