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Clinical characteristics and outcomes of systemic lupus erythematosus patients admitted to Assiut University Hospital critical care unit

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Abstract

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that may cause severe complications. This study aimed to investigate the frequency of critical complications in SLE patients requiring intensive care unit (ICU) admission and to identify potential risk factors affecting their outcomes. The study included 50 SLE patients admitted to the Critical Care Unit. All patients underwent a comprehensive medical history, physical examination and laboratory investigations. Disease activity was assessed using the modified new version of the SLE disease activity index (SLEDAI-2K). Both the Acute Physiology and Chronic Health Examination-II (APACHE-II) score and the Sequential Organ Failure Assessment score (SOFA score) were calculated within 24-hour period post-admission. Patients were followed until hospital discharge or demise. The mean age of the studied patients was 33.62 years, with a range of 20 to 47 years. The most leading causes of admission were lupus nephritis (44%) and pneumonia (24%). Of these patients, 12 (24%) patients developed different forms of complications. Of the patients, 80% survived, while 20% experienced a fatal outcome. The predictors of mortality were older age (odds ratio 1.59), complications (odds ratio 2.09), and high APACHE-II scores (odds ratio 3.11). In conclusion, patients with SLE admitted to the critical care unit were liable for complications in the presence the following risk factors; old age, high disease activity and high APACHE-II.

Keywords: Systemic lupus erythematosus, outcomes, intensive care unit, complications, mortality.

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Introduction

Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disorder with a diverse clinical manifestations and variable severity, affecting individuals of all ages and ethnicities. Child-bearing women are particularly susceptible.[1]

Despite advancements in treatment, SLE remains a significant cause of intensive care unit (ICU) admissions among rheumatic diseases. While the overall survival has improved, patients with life-threatening conditions continue to face a challenging prognosis. A number of studies have focused on the clinical characterization and outcomes of SLE patients

in critical conditions.[2,3] Ethnic differences, health-care referral systems, and availability of therapy may influence SLE manifestations and prognosis. However, there is a paucity of research offering a detailed clinical profile of SLE patients requiring ICU admission. Moreover, existing data on factors predicting patient outcomes in this population are discordant.[2, 3] This study aimed to identify the primary causes of ICU admission and evaluate the outcomes of SLE patients, also to emphasize the importance of early diagnosis, risk stratification, and personalized treatment in improving outcomes for SLE patients.

Materials and Methods

This was a prospective hospital-based study, conducted at the Critical Care Unit within the Department of Internal Medicine at Assiut University. The study period spanned from June 2022 to June 2023. The study included 50 adult patients (aged 18 years and older) diagnosed with SLE, who presented to the Department of Emergency, Assiut University Hospital. All participants fulfilled the SLE classification criteria of the European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) 2019 [4].

Exclusion Criteria

Any patient with one or more of the following conditions was excluded from the study. These included patients with a stay in the ICU of less than 48 hours, patients with significant chronic organ disease unrelated to SLE, patients with terminal cancer or other autoimmune diseases.

Methods

All enrolled patients underwent a comprehensive history and physical examination. Demographic data and prior ICU admissions were recorded.

Laboratory tests included

Complete blood count (CBC); Liver function tests: including total protein, albumin, liver enzymes (alanine transaminase (ALT), aspartate transaminase (AST)); Kidney function tests: including urea, creatinine, albumin-to-creatinine ratio, 24-hour urinary proteins, and glomerular filtration rate; and Complement 3 (C3), and complement 4 (C4) were performed using an automated hematology and blood chemistry machine (Sysmex XN 1000 System, Siemens, Germany), according to the manufacturer's instructions.

Erythrocyte sedimentation rate (ESR) was measured by the Westergren method. And, C-reactive protein (CRP) was assessed using an indirect immunofluorescence method by commercial kits (Kallestad™ CRP kits, manufactured by Bio-Rad Laboratories, Hercules, USA), according to the manufacturer's instructions.

Disease activity was evaluated using the Modified New versions of the SLE disease activity index (SLEDAI-2K). SLEDAI-2K scores were categorized as follows: no activity (SLEDAI score of 0), mild activity (SLEDAI score of 1-5), moderate activity (SLEDAI score of 6-10), high activity (SLEDAI score of 11-19), and very high activity (SLEDAI score of 20 or higher) [5]. The Acute Physiology and Chronic Health Examination-II (APACHE-II) score was assessed within 24 hours of admission; with elevated scores indicate a more severe disease state and an elevated risk of mortality. The Sequential Organ Failure Assessment score (SOFA score) was also calculated, ranging from 0 (best) to 24 (worst) [6]. Patients were followed until discharge or death.

Statistical Analysis

Data were analyzed with the Statistical Package for Social Sciences (SPSS) version 20 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Continuous variables are presented as mean and standard deviation (SD) and compared using the Student's t-test. Nominal data are expressed as frequency (percentage) and compared using the Chi-square test. Predictors for complications were determined through logistic regression analysis. The area under the curve (AUC) of the receiver operator characteristics (ROC) curve was used to evaluate the discriminative ability of different predictors for predicting complications and mortality. A p-value <0.05 was considered significant.

Results

Baseline data and causes of admission among studied patients

The mean age of the studied patients was 33.62 ± 8.23 years (range 20-47 years). Of the 50 patients, 40 (80%) were females and 10 (20%) males. The leading causes of admission to ICU were lupus nephritis-related conditions (44%), including volume overload, pulmonary edema, renal failure, and hypertensive emergency. Other causes included serositis (8 cases, 16%), myocarditis (5 cases, 10%), and lupus cerebritis (3 cases, 6%). Twelve patients (24%) had a history of previous ICU admission.

Baseline laboratory data among the studied patients

Table 1 shows baseline laboratory data among the studied patients. The mean APACHE-II score was 34.09 ± 10.87 while the mean SOFA score was 11.08 ± 3.98.

Table 1. Baseline laboratory data among the 50 studied patients.

	N= 50
Hemoglobin (g/dl)	10.87 ± 2.22
Leucocytes (10^3/ul)	7.85 ± 4.95
Platelets (10^3/ul)	227.61 ± 125.41
INR	1.12 ± 0.30
Bilirubin (mmol/l)	12.09 ± 2.11
Aspartate transaminse (ul/l)	49.64 ± 14.45
Alanine transaminse (ul/l)	69.66 ± 16.09
Albumin (g/dl)	35.11 ± 5.39
Urea (mg/dl)	12.08 ± 2.11
Creatinine (mg/dl)	2.76 ± 1.99
ESR (ml/h)	75.67 ± 22.19
CRP (mg/dl)	32.19 ± 5.58
Complement 3 (mg/dl)	22.01 ± 3.09
Complement 4 (mg/dl)	3.89 ± 1.55
APACHE-II score	34.09 ± 10.87
SOFA score	11.08 ± 3.98

Data are expressed as mean (±SD). INR: intrantional randomized ratio; ESR: erythrocyte sedematation rate; CRP: C-reactive protein; APACHE-II: Acute Physiology and Chronic Health Evaluation; SOFA: sequential organ failure assessment score.

Complications among the studied patients

The majority of patients (76%) did not develop complications. Of the studied patients, 12 patients (24%) experienced various complications, including pulmonary embolism (6 cases, 12%), gastrointestinal bleeding (3 cases, 6%), seizures (2 cases, 4%), and disseminated intravascular coagulation (DIC) (1 case, 2%).

Length of stay, treatment and outcome among the studied patients

The mean length of stay in the ICU was 15.98 ± 2.98 days. All patients received steroids in varying doses and hydroxychloroquine (400 mg daily) prior to admission, and 15 (30%) also took azathioprine. Of the study patients 35 cases (70%) were treated with antibiotics, and 6 cases (12%) received low molecular weight heparin (LMWH). Of the total cohort, 40 patients (80%) survived, while 10 patients (20%) deteriorated and experienced a fatal outcome. The most common causes of death were shock (3 cases, 30%), sepsis (1 cases, 10%), pulmonary complications (4 cases, 40%), and renal failure (2 cases, 20%).

Predictors of complications in the current study

Data are shown in Tables 2, 3 and Figure 1**.** Among the studied patients, older age (Odds ratio (OR) 1.98), SLE Disease Index (SLEDAI-2k: 1.23), lupus cerebritis (OR: 2.30), and APACHE-II score (OR: 3.89) were identified as predictors of complications. For predicting complications in these patients, an APACHE-II score cutoff of >29 demonstrated 82% sensitivity, 94% specificity, an overall accuracy of 88.2%, at an area under the curve (AUC) of 0.853.

Table 2. Predictors of complications in the current study.

	Odd's ratio	95% CI	*p* value
Age (years)	1.98	1.34-4.01	0.03
Lupus cerebritis	2.30	2.01-6.78	< 0.001
Albumin (g/dl)	1.11	0.22-3.01	NS
Complement C3	0.89	0.33-1.90	NS
Complement C4	1.09	0.55-2.18	NS
SLEDAI-2k	1.23	1.10-2.90	0.01
SOFA score	1.22	0.97-3.19	NS
APACHE-II	3.89	2.77-8.69	< 0.001

CI: confidence interval; SOFA: sequential organ failure assessment score; APACHE-II: Acute Physiology and Chronic Health Evaluation. *p* > 0.05 is not significant (NS).

Table 3. Accuracy of APACHE-II in prediction of complications in the current study.

Indices	Value
Sensitivity	82%
Specificity	94%
Positive predictive value	93%
Negative predictive value	85%
Accuracy	88.2%
Cutoff point	> 29
Area under curve	0.853
p value	< 0.001

Data are presented according to the receiver-operating characteristic (ROC) curve analysis; *p* value is significant at < 0.05.

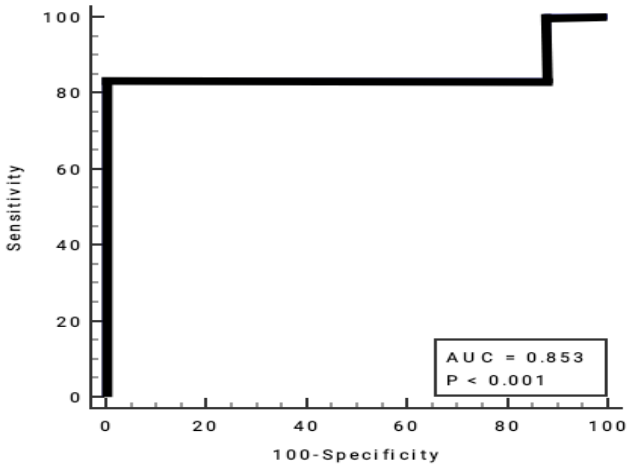

Figure 1. Receiver operator characteristics (ROC) curve analysis for APACHE-II score in prediction of complications. APACHE-II: Acute Physiology and Chronic Health Evaluation; AUC: area under curve**.**

Predictors of mortality in the current study

Data are shown in Tables 4, 5 and Figure 2. Older age (OR: 1.59), complications (OR: 2.09), and APACHE-II score (OR: 3.11) were identified as predictors of mortality among the studied patients. For predicting mortality in these patients, an APACHE-II score cutoff of >32 demonstrated 83.3% sensitivity, 100% specificity, an overall accuracy of 91.4%, at an area under the curve (AUC) of 0.842.

Table 4. Predictors of mortality in the current study.

	Odd's ratio	95% CI	*p* value
Age (years)	1.59	1.40-3.76	0.03
Complications	2.09	1.11-5.01	0.01
Leucocytosis	1.22	0.87-2.56	NS
Albumin (g/dl)	0.98	0.44-1.98	NS
Complement C3	1.01	0.66-2.03	NS
Complement C4	1.20	0.80-2.87	NS
SOFA score	1.33	0.77-2.66	NS
APACHE-II	3.11	2.01-9.11	< 0.001

Data are presented according to the logistic regression analysis; CI: confidence interval; SOFA: sequential organ failure assessment score; APACHE-II: Acute Physiology and Chronic Health Evaluation. $p > 0.05$ is not significant (NS).

Table 5. Accuracy of APACHE-II in prediction of mortality in the current study.

Indices	Value
Sensitivity	83.3%
Specificity	100%
Positive predictive value	100%
Negative predictive value	85%
Accuracy	91.4%
Cutoff point	> 32
Area under curve	0.842
p value	< 0.001

Data are presented according to the receiver-operating characteristic (ROC) curve analysis. *p* value is significant at < 0.05.

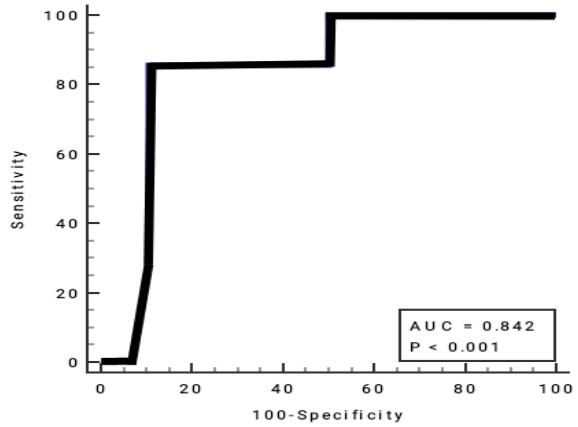

Figure 2. Receiver operator characteristics (ROC) curve analysis for APACHE-II score in prediction of mortality. APACHE-II: Acute Physiology and Chronic Health Evaluation; AUC: area under curve.

Discussion

Prompt diagnosis and timely management are crucial for minimizing morbidity and mortality in SLE patients with complications.[7, 8] Differentiating between SLE flares and complications can be challenging, especially for primary care or emergency physicians, leading to potential delays in diagnosis and treatment.[9,10]

Given these considerations, we conducted a study to investigate the clinical characteristics and identify risk factors associated with complications and mortality among SLE patients admitted to the ICU. We enrolled 50 patients with SLE. The mean age was 33.62 years, and 80% of patients were female, consistent with a previous study.[11]

The most common causes of hospitalization among our study population were lupus nephritis (44%) and pneumonia (24%). In a previous study of 60 SLE patients, cardiogenic causes, pneumonia, sepsis, and lupus cerebritis were identified as leading causes of ICU admission.[12]

Namendys-Silva et al., 2009, found that different infections were the primary reason for ICU admission in most SLE patients (61.5%), these included lupus nephritis and lupus cerebritis.[13] A systematic review also identified infections as the leading cause of admissions, followed by pulmonary and renal complications.[14]

In our study, the majority of patients (76%) did not develop complications. However, 12 (24%) patients experienced various complications, including pulmonary embolism, gastrointestinal bleeding, seizures, and disseminated intravascular coagulation (DIC). Of these patients, 40 (80%) survived, while 10 (20%) deteriorated and died.

Previous studies reported a gastrointestinal hemorrhage incidence of 3.5-5% in the general ICU population.[15, 16] Our findings suggested a significantly higher incidence of gastrointestinal bleeding among SLE patients (29.4%) compared to the general cohort.

Based on our analysis, predictors of mortality among SLE patients included older age, complications, and the APACHE-II score. For predicting complications, an APACHE-II score greater than 32 had a sensitivity of 91.4%. Additionally, older age, lupus cerebritis, SLEDAI, and APACHE-II were identified as predictors of complications.

The study by Hsu et al., 2005 and Ñamendys-Silva et al., 2009, identified seizures as a major complication of ICU admission.[12, 13] Infections, including septic shock, pneumonia, central nervous system (CNS) infections, and endocarditis were the primary causes of mortality (42%), as showed in a previous study,[17] aligning with findings from studies in both developing[13, 18, 19] and developed countries.[20]

Older age, complications, and APACHE-II score showed statistical significance as risk factors for mortality among our studied patients. An APACHE-II score greater than 29 had an accuracy of 88.2%. Zamir et al., 2018, reported an overall mortality rate of 29.6% in SLE patients admitted to the general ICU. They found that APACHE II score, bacteremia, and infection with gram-negative bacteria were predictors of mortality. The ROC analysis of the APACHE II score revealed an AUC of 0.82 with a cutoff point greater than 27, demonstrating a sensitivity of 83.3 and a specificity of 84.2.[21]

APACHE II, an additional substantial predictor of death in our population, demonstrated a high association with mortality at a score of 32. Up to now, APACHE II remains the most commonly used variable for predicting mortality in SLE patients.[18, 22, 23] However, a study conducted in Mexico City found that APACHE II demonstrated poor performance in predicting mortality with an area under curve of 0.689 (95% CI 0.586-0.791), but showed good calibration.[13] The discrepancies observed between our findings and those of previous studies may be explained by the lack of standardization in the risk factors analyzed and the diverse nature of the studies.

Our study revealed that the SOFA score lacked predictive value for mortality. While two previous studies assessed the SOFA score in SLE patients, their findings differed regarding its association with mortality.[24, 25]

One of the limitations of this study is its relatively small sample size. Additionally, our patients received conventional immuno-suppressive therapies, and the impact of biological drugs like belimumab or rituximab on survival was not evaluated.

In conclusion, our study highlighted the significance of early diagnosis, risk stratification, and personalized treatment in improving outcomes for SLE patients admitted to the ICU. Based on our findings, predictors of complications among the studied patients were old age, SLEDAI-2K, and lupus cerebritis. Meanwhile, predictors of mortality included old age, complications, and APACHE-II. By implementing these recommendations, healthcare providers can contribute to reducing mortality and improving the overall quality of life for individuals with SLE.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by MFH, SElA, ABA and SSE. The first draft of the manuscript was written by EMI and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval

The study protocol was reviewed and approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Assiut University, Assiut, Egypt. The IRB local approval number is 17101709 (dated April, 2022). The trial was registered in clinicaltrials.gov on June 13, 2022. The trial registration number (TRN) is NCT055418855.

Informed consent

All participants gave their informed written consent prior to their inclusion in the study.

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