Prognosis of patients with systemic lupus erythematosus in the intensive care unit

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Abstract

Introduction: Identification of risk factors for mortality has enabled improving the treatment of critically ill patients with systemic lupus erythematosus. **Objective:** To describe clinical characteristics and prognoses of critically ill patients with systemic lupus erythematosus admitted to an intensive care unit. **Method:** Prospective, observational cohort study. A total of 207 patients with systemic lupus erythematosus admitted between January 2011 and January 2016 were included. **Results:** During the study period, 3,215 critically ill patients were admitted to the intensive care unit, out of which 207 (6.4%) were identified as having systemic lupus erythematosus after being evaluated by an intensivist. The multivariate analysis identified the presence of organ failure (cardiovascular, liver, neurological) and serum lactate levels > 2 mmol/L at admission or within the first 24 hours of intensive care unit stay as the main factors associated with increased mortality. **Conclusions:** A relevant observation was that neurological failure and liver failure were associated with higher mortality risk at 28 days, without reports similar to these findings being identified.

KEY WORDS: Lupus. Antiphospholipid syndrome. Intensive care.

Introduction

Systemic lupus erythematosus (SLE) is a rheumatologic polymorphic disease where there is autoimmunity in all organs and it is characterized by exacerbations and remissions.¹ It is a pro-inflammatory pathology where the patient is predisposed to infections during the exacerbation states, which can cause life-threatening clinical conditions.^{2,3} On the other hand, immunosuppressive treatment can increase the risk of systemic complications.⁴

Although there are no precise statistical data, prevalence of SLE is high worldwide, with a trend to increase.^{5,6} In spite of the above, mortality has decreased in recent decades, probably owing to earlier diagnosis and higher availability of immunosuppressive treatments.⁷⁻⁹ In severely ill patients with SLE who require admission to an intensive care unit (ICU),

cardiovascular failure remains one of the main risk factors for death.^{10,11} In some series, the following death predictors have been identified in critical patients with SLE: respiratory system infections, APACHE II high score, need for renal replacement therapy, use of mechanical ventilation and SLEDAI high score.^{12,13} The identification of risk factors for mortality has allowed to improve the treatment of critical patients with SLE.^{14,15} The purpose of the present work was to describe the clinical characteristics and prognosis of critically ill patients with LEG admitted to an ICU.

Method

Descriptive, analytical, observational study carried out at the ICU of Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán", between January 2011 and January 2016. The UCI has 14 beds to take

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care of seriously ill patients and has the capability to provide advanced support such as invasive mechanical ventilation, hemodialysis and plasmapheresis. All severely ill patients with SLE, of either gender, older than 16 years, who remained in the ICU for more than 24 hours were included. Demographic and clinical data were obtained from the clinical record and the electronic file. The patients met the criteria for SLE upon ICU admission or were classified as having SLE during their stay at the ICU.

The following data were recorded: age, gender, time since SLE diagnosis, steroid dose at ICU admission, diagnosis for admission to the unit, days of stay in it, place of provenance, APACHE II¹⁶ score and SOFA¹⁷ score upon ICU admission, as well as number of SOFA-defined organ failures.¹⁸ In addition, the need for vasopressors, required dose, serum lactate at admission, PaO₂/FiO₂ at admission to the ICU, need for mechanical ventilation (MV) and reason, days of MV, creatinine level, platelet count and bilirubin levels were recorded. Additionally, the presence of clinical or serological secondary antiphospholipid syndrome (APS) and the score on the Glasgow Coma Scale (GCS) prior to receiving sedation, if required, were recorded.¹⁶⁻²⁰ Mortality was recorded at 7 and 28 days of UCI discharge.

Statistical analysis

Descriptive statistics was used for data presentation and the Kolmogorov-Smirnov test was used to determine their distribution. Numerical variables were expressed as median and interquartile ranges, given that all continuous variables showed a non-parametric distribution; nominal variables were represented as numbers and percentages.

Cox univariate and multivariate regression analysis was used to identify factors related to mortality increase at 28 days. Variables with clinical relevance and those predictive of the primary endpoint in the univariate analysis were introduced in the final model. The results were expressed as hazard ratios with their respective 95 % confidence intervals. Survival curves were estimated using the Kaplan-Meier method. Survival data were compared with the log-rank test. In all cases, a p-value < 0.05 was considered to be statistically significant. For the processing of data, the statistical program SPSS 22.0 was used.

The present study adhered to the considerations formulated in the Declaration of Helsinki and its Tokyo amendment for biomedical research works in human

Table 1. General characteristics of 207 patients with systemic lupus erythematosus admitted to an intensive care unit

Variable	n	%
Gender		
Female	184	(88.9)
Male	23	(11.1)
Provenience		
Emergency department	160	(77.3)
Hospitalization	47	(22.7)
28-day mortality	38	(18.4)
	Median	IQR
Age (years)	31	24-43
APACHE II (score)	19	(14-24)
SOFA (score)	8	(6-11)
Time since diagnosis (years)	7	(2-13)
Prednisone dose (mg/day)	16	(5-50)
Days of ICU stay	4.5	(3-10)
Lactate (mmol/L)	2.0	(1.2-2.9)
PaO ₂ /FiO ₂ , mmHg	180	(120-260)
Creatinine (mg/dL)	2.0	(1-4.8)
Total bilirubin (mg/dL)	1.21	(0.9-1)
Platelets x 10 ³ /mm ³	112	(57-112)

IQR = Interquartile range.

subjects, as well as to the considerations regarding research for health formulated in the General Statute of Health of the Mexican United States. Since this was an observational study, written informed consent from the patients was not necessary.

Results

During the study period, 3215 seriously ill patients were admitted to the ICU, among them 207 (6.4 %) with SLE after being evaluated by an intensivist. Median age was 31 years, and 88.9 % were of the female gender. Median time since SLE diagnosis was 7 years. The characteristics of the patients included in the study are shown in Table 1.

A total of 74.4 % of patients were admitted due to a medical problem: infectious (46.4 %), cardiovascular (16.9 %) and neurological (10.5 %) in nature. The most commonly observed organ failures were kidney (71.5 %), hematologic (64.3 %) and respiratory failure (62.8 %). MV was required by 77.8 % of patients; mean duration was 6 days. Mortality was 18.4 % (38/207). Mortality of patients with 4 or more organ failures was 39.7 % (29/73). Table 2 shows the

Table 2. Relationship between the number of organ failures and 28-day mortality in patients with systemic lupus erythematosus admitted to an intensive care unit

Failures			Mortality	
Number	n	%	n	%
0	2	1	0	0
1	34	16.4	1	2.9
2	41	19.8	1	2.4
3	57	27.5	7	12.3
4	46	22.2	13	28.2
5	23	11.1	14	60.8
6	4	1.9	2	50

relationship between the number of organ failures and 28-day mortality.

Of the patients who experienced respiratory failure, 20 (9.7 %) had a diagnosis of diffuse pulmonary hemorrhage (DPH) and 14 met the criteria for acute respiratory distress syndrome (ARDS) (6.8 %). 28-day mortality of patients with respiratory failure was 28.6 % (4/20).

Tables 3 and 4 show detailed results of the univariate and multivariate analyses to identify the factors associated with mortality increase at 28 days. The factors associated with 28-day mortality increase were cardiovascular failure (HR = 3.27, 95% CI = 1.41-7.54, $p = 0.005$), liver failure (HR = 2.16, 95% CI = 1.11-4.22, $p = 0.024$), neurological failure (HR = 3.42, 95% CI = 1.75-6.68, $p < 0.001$) and serum lactate levels (HR = 1.17, 95% CI = 1.06-1.29, $p = 0.002$) (Table 4 and Figure 1).

Discussion

The main findings of the present study were:

- Mortality of severely ill patients with LEG admitted to the ICU was 18.4%.
- The main factors associated with 28-day mortality increase were neurological, cardiovascular and liver failures.
- Lactate levels at ICU admission or during the first 24 hours of stay constitute a biomarker of risk for death in severely ill patients with SLE.

Different groups have reported mortality decreases in patients with SLE over the course of the last decade, which may be related to an improvement in SLE treatment and technological advances in intensive care, in addition to early admission to the ICU having

Table 3. Univariate analysis to identify factors related to 28-day mortality in patients with systemic lupus erythematosus admitted to an intensive care unit

Variable	HR	95 % CI	p
Age (years)	1.03	1.01-1.06	0.001
Male gender	0.41	0.10-1.73	0.230
APACHE II	1.11	1.07-1.16	< 0.001
SOFA	1.37	1.25-1.51	< 0.001
Cardiovascular failure	5.8	2.66-12.6	< 0.001
Lactate (mmol/L)	1.28	1.17-1.39	< 0.001
Lactate > 2 mmol/L	2.45	1.27-4.75	0.008
Respiratory failure	1.69	0.82-3.48	0.154
PaO ₂ /FiO ₂ (mmHg)	0.99	0.99-1.0	0.104
Kidney failure	1.12	0.54-2.32	0.741
Hematological failure	2.66	1.17-6.04	0.019
Liver failure	3.44	1.82-6.52	< 0.001
Neurological failure	4.07	2.12-7.81	< 0.001
APS	0.72	0.35-1.46	0.367
ARDS	1.62	0.57-4.57	0.360
DPH	0.48	0.11-2.0	0.317

HR = Hazard ratio, APACHE = Acute Physiology and Chronic Health Evaluation, SOFA = Sequential Organ Failure Assessment, APS = Anti-phospholipid syndrome, ARDS = Acute respiratory distress syndrome, DPH = Diffuse pulmonary hemorrhage.

been internationally promoted with a lower number of organ failures. Overall mortality in the present work was lower than that reported by other centers.^{13,21} Dumas et al.¹¹ reported a mortality rate of 20 % in rheumatologic patients, similar to that found in the present work.

APACHE II and SOFA¹⁶⁻¹⁹ scores of have been associated with higher mortality in seriously ill patients with SLE. Our group¹⁰ reported that the APACHE II score was 19.7 during the first 24 hours of ICU stay, similar to that of the present report. Other authors have reported higher APACHE II scores and higher mortality.¹³

Few studies have used the SOFA score to determine if a patient with SLE is admitted or not to the ICU; in the present work, it was included and was identified as a risk factor for death. Other authors,¹¹ in spite of not categorizing the SOFA scores by organ failures, have reported lower scores in comparison with the score in our group of patients with SLE (5 versus 8 points), which suggests that in the ICU of our center patients with larger number of organ failures or higher severity are admitted; however, in spite of this difference in the SOFA score, mortality was similar (21 % versus 18.3 %).

Figure 1. Survival curves according to 28-day mortality-associated factors in patients with systemic lupus erythematosus admitted to an intensive care unit.

Table 4. Multivariate analysis to identify factors related to 28-day mortality in patients with systemic lupus erythematosus admitted to an intensive care unit

Variable	HR	95 % CI	p
Cardiovascular failure	3.27	1.41-7.54	0.005
Liver failure	2.16	1.11-4.22	0.024
Neurological failure	3.42	1.75-6.68	< 0.001
Lactate > 2 mmol/L	1.17	1.06-1.29	0.002

HR = Hazard ratio.

Conclusions

When the number and type of organ failures patients were admitted with were assessed, similar results to those of other studies were found,¹⁰⁻¹³ with cardiovascular failure being one of the main risk factors for death. Although in our group of patients the organ failure with the highest prevalence was kidney failure, it had no impact on mortality. One relevant finding was that neurological failure and liver failure were associated with higher risk of death at 28 days; in this sense, there are no reports similar to our results. Neurological alterations of severely ill patients with sepsis, vascular events or epileptic states were the main causes of neurological involvement in our cohort.^{22,23} Patients with SLE and neurological alteration have been described to have

high mortality;²⁴ therefore, they require surveillance in monitored areas in order to improve the prognosis. Finally, similar to reports by other authors,^{25,26} serum lactate level during the first 24 hours of UCI stay was associated with higher mortality.

The main limitation of the present study lied in that it was carried out in a single center with high concentration of patients with immune diseases.

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