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Clinical and epidemiologic characterization of patients with systemic lupus erythematosus admitted to an intensive care unit in Colombia

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Abstract

Objective: Describe the clinical and epidemiologic characteristics of patients with systemic lupus erythematosus (SLE) admitted to the intensive care unit (ICU).

Methods: a retrospective study with medical records review of patients with systemic lupus erythematosus (SLE) admitted to the ICU between 2004 and 2015 were included. Qualitative variables were described using absolute and relative frequencies. For quantitative variables mean value and standard deviation (SD) or median value with the interquartile range (IQR) depending on data distribution. To compare groups, it was used the Student t-test or Mann Whitney U test as appropriate and Fisher's exact test.

Results: 33 patients were included, with a total of 45 ICU admissions, 29 (87.9%) were females with a median age of 26 years. The median time of diagnosis of SLE was two years, (IQR 1.5–5). The most common SLE manifestation and comorbidity were renal disease and hypertension with 27 (81.8%) and 14 (42.4%) respectively. The main reason for admittance was lupus flare with 25 events (55.5%). Infection was the second cause of admission with 19 events (42.2%). The median stay time in the ICU was four days (IQR 2–7). LODS score was 6 (RIQ 5–8), and APACHE II score was 13 (RIQ 11–17.7). There were 29 infections (64.5%) of which 20 (69%) were hospital-acquired. Four (12.1%) patients died.

Conclusion: Unlike most of the previously reported series, in this study SLE activity was the most common cause of admission in the ICU. A more aggressive disease and difficulties in the ambulatory setting could explain this behavior. Despite the higher percentage of lupus flares, there was lower mortality.

Keywords: Lupus erythematosus, Systemic, Intensive care unit, Symptom flare up, Infection, Mortality

Introduction

Rheumatological diseases (RD) are a heterogeneous group of entities with a chronic course and multisystemic involvement associated with significant morbidity and mortality. The complexity of the management of these diseases in the intensive care unit (ICU) lies in the fact that their complications do not derive only from the activity of RD, but from other associated factors such as the side effects of

treatment and the lower functional reserve derived from cumulative damage to this type of diseases [1, 2].

Historically, patients with rheumatoid arthritis (RA) have occupied the first place of RD admitted to the ICU [3]. However, this has changed in recent decades secondary to therapeutic advances that have allowed better control of the disease and less dependence on steroidal therapy and non-steroidal anti-inflammatory drugs (NSAIDs). This has led to less prevalent diseases such as systemic lupus erythematosus (SLE) occupy their place as a cause of admission to ICU within the RD [3–5], generating a knowledge gap, which is particularly important given that the behavior of SLE differs significantly from other ERs.

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At the local level, few studies provide information on patients with SLE and admission to the ICU, and those that do exist to RD in general [2, 6–9]. It is therefore essential to have data of SLE in Latin America since certain factors vary with a geographic location such as race and access to health services that can significantly affect the prognosis of this disease [10, 11]. Additionally, the therapeutic advances in the different rheumatological diseases have not been the same, which accentuates the differences between them.

The objective of this study is to define the epidemiological and clinical characteristics of patients with SLE who enter to ICU in a reference hospital, with experience in the management of autoimmune diseases in the city of Medellin, Colombia. This study will serve to determine the characteristics of patients that enter to ICU and plan management strategies.

Patients and methods

Study design and patient selection

A retrospective descriptive study of medical records from adult patients with SLE admitted to ICU at Clinica Universitaria Bolivariana (CUB) (Medellin, Colombia) between the years 2004 and 2015. The inclusion criteria were: patients over 18 years of age, diagnosed with SLE according to the classification criteria of ACR [12], admitted to the ICU during the study period. We excluded patients with concomitant oncological diseases, transplanted with active graft and immunosuppressive therapy and those whose records of clinical history were incomplete for the variables of interest.

Data collection

The information was obtained through the review of the physical and electronic histories of patients who met the eligibility criteria of the study and was recorded in an electronic format (Magpi) designed considering the study variables (at admission, hospital stay and discharge from the ICU). A pilot test was carried out with ten clinical histories to assess the quality of the form and the need to adjust. The data was collected by two researchers if there were missing information in the selected ICU records; the data was searched in the laboratory results, nurse registry, and the patient's treatment specialties notes.

The variables that were investigated in the registries to fulfill the objectives of the study were demographic, clinical, treatment and outcomes (conditions of discharge, overall mortality, days of ICU stay, nosocomial infections, surgical interventions required). For the sepsis criteria, the Surviving Sepsis 2012 guidelines were considered [13], the renal failure was diagnosed according to the diagnostic criteria of acute kidney injury of KDIGO 2012 [14].

Statistical analysis

To describe the qualitative variables, absolute and relative frequencies were used and for the quantitative variables mean and standard deviation (SD) or the median with interquartile range (RIQ) were used depending on the distribution of the data. To compare groups it was used the Student t-test or Mann Whitney U test as appropriate and Fisher's exact test. *P* values < 0.05 were considered statistically significant. All the analyses were carried out in the statistical package IBM SPSS version 24.

Results

Demographic characteristics and comorbidities

A total of 959 records were reviewed, of which 33 patients met the eligibility criteria, presenting 45 episodes of admission to the ICU. Of the 33 patients, 29 (87.9%) were female, with an median age of 26 years. Regarding comorbidities, 21 (63.6%) had at least one comorbidity at the time of admission to the ICU, the most frequent being arterial hypertension 14 (42.4%), followed by chronic kidney disease (18.1%) (Table 1).

Baseline characteristics

The median time of SLE diagnosis was two years (RIQ 1–5.5 years), the most frequent clinical manifestation was renal involvement, in 27 patients (81.8%), followed by joint in 19 (57.6%). Regarding the place from which the patients were transferred to the ICU, most of them entered from the emergency department, 19 (57.6%) patients. Eleven patients (33.3%) were referred from other institutions, and four patients (12.1%) had had a previous hospitalization, mainly due to disease activity. The most frequent

Table 1 Demographic characteristics of SLE patients admitted to the ICU

Characteristic	<i>N</i> = 33 <i>n</i> (%)
Female sex	29 (87,9)
Age ^a	26 (23–35)
Comorbidities	21 (63,6)
• Arterial hypertension	14 (42,4)
• Chronic renal failure	6 (18,1)
◦ Dialysis	3
• Hypothyroidism	5 (15,1)
• Cerebrovascular disease	5 (15,1)
• Tuberculosis	3 (9,0)
• Diabetes	2 (6,0)
• Cardiac failure	1 (3,0)
• Asthma	1 (3,0)
• Peripheral artery disease	1 (3,0)

^aMedian/Interquartile range (IQR)

ambulatory therapeutic strategy was steroids 28 (84.8%), followed by antimalarials 22 (66.6%). (Table 2).

Clinical and paraclinical characteristics upon admission to the ICU

During the evaluated period there were 45 ICU admissions, corresponding to 33 patients, from this moment onward we will refer to the 45 admission events. The leading cause of admission was disease activity with 25 events (55.5%), followed by infection with 19 events (42.2%). The most frequent organic involvement was renal with 24 events (53.3%) explained mainly by lupus nephritis (Table 3). Table 4 shows the vital signs and the paraclinical signs on admission. The calculation of the SELENA SLEDAI was possible only in 23 events, with an average score of 20 (SD 11).

When comparing at baseline the patients who presented infection (Table 5) versus those who did not, it was found that the APACHE was higher, as well as the CRP, other variables such as the time of diagnosis of the disease, type of baseline commitment or the previous use of steroids were not more at the time of admission due to infection. When comparing at baseline patients

Table 2 Baseline clinical characteristics

Baseline clinic characteristics	N = 33 n (%)
Disease diagnosis time in years ^a	2 (1–5,5)
SLE manifestation	
• Renal	27 (81,8)
• Articular	19 (57,6)
• Hematological	19 (57,6)
• Mucocutaneous	18 (54,5)
• Serositis	8 (24,2)
• Central Nervous System	8 (24,2)
• Pulmonary	4 (12,1)
Previous hospitalization	28 (84,8)
Previous hospitalization days ^a	5 (1–15)
Previous ICU admission	4 (12,1)
Outpatient treatment	
• Steroids	28 (84,8)
• Chloroquine	22 (66,6)
• Rituximab	4 (12,1)
• Azathioprine	4 (12,1)
• Mycophenolate	4 (12,1)
• Cyclophosphamide	2 (6,0)
• Methotrexate	1 (3,0)
• Leflunomide	1 (3,0)
• Calcineurin inhibitors	1 (3,0)

^aMedian/Interquartile range (IQR)

Table 3 Clinical characteristics upon admission to ICU in 45 events

Clinical characteristics upon admission to ICU	N = 45 n (%)
Reasons for UCI admission	
• Disease activity	25 (55,5)
• Infection	19 (42,2)
• Ventilatory failure	18 (40,0)
• Cardiovascular emergency	12 (26,7)
• Hemorrhage	7 (15,5)
• Dialytic urgency	6 (13,3)
• Postsurgery care	5 (11,1)
Organic commitment	
• Renal involvement	24 (53,3)
• Haematological commitment	19 (42,2)
◦ Hemolytic anemia	13 (28,9)
◦ Thrombocytopenia	13 (28,9)
◦ Lymphopenia	10 (22,2)
◦ Neutropenia	6 (13,3)
• Lung commitment	18 (40,0)
◦ Acute Pulmonary Edema	8 (17,8)
◦ ARDS ^a	5 (11,1)
◦ Pleural effusion	4 (8,9)
◦ Alveolar hemorrhage	4 (8,9)
◦ Pneumonitis	3 (6,7)
◦ Pulmonary embolism	1 (2,2)
• Commitment of CNS ^b	9 (20,0)
◦ Vasculitis	4 (8,8)
◦ Hemorrhage	2 (4,4)
◦ Optic neuritis	1 (2,2)
◦ Myelopathy	1 (2,2)
◦ Autoimmune encephalitis	1 (2,2)
• Cardiac commitment	5 (11,1)
◦ Myocarditis	1 (2,2)
◦ Pericarditis	4 (8,9)
• Gastrointestinal commitment	5 (11,1)
◦ Hepatitis	4 (8,9)
◦ Digestive tract hemorrhage	1 (2,2)
◦ Pancreatitis	1 (2,2)

^aAcute Respiratory Distress Syndrome, ^bCNS central nervous system

who were admitted for disease activity with those who did not (Table 5), more renal involvement, hemolytic anemia, and thrombocytopenia were found.

Management during the stay in ICU

Antibiotics were used in 31 (68.9%) of the 45 admissions with carbapenems and piperacillin/tazobactam as the most

Table 4 Vital signs and laboratory upon admission to the ICU

Vital signs and laboratory	N = 45 Media (SD)
Heart rate (bpm)	101 (22,1)
Systolic pressure (mmHg)	126 (39,0)
Diastolic pressure (mmHg)	77 (23,6)
PaFi	313 (158,8)
Hemoglobin (g / dL)	9,2 (2,3)
INR	1,14 (0,2)
Apache II ^a	13 (11–17,7)
SLEDAI ^b	20 (11,0)
LODS Score ^a	6 (5–8)
Creatinine (mg / dL) ^a	1,3 (0,8–3,55)
Platelets (cel / mm3)	204593 (116.000)
CRP ^a	5,0 (2,4–11,0)
Glasgow	
• < 15	9 (20,0)
• 15	36 (80,0)

^aMedian (RIQ), ^bIt could only be taken in 23 patients, CRP c reactive protein

frequently used in 15 (33.1%) and 12 (26.7%) respectively. Treatment for tuberculosis was used in three cases (6.7%) and seven (15.5%) received antifungal treatment. Immunosuppression was mainly used in the form of pulses of methylprednisolone in 22 admissions (48.9%). Concerning

additional supports, mechanical ventilation was used in 14 cases (31.1%), hemodialysis in 16 events (35.5%) and the latter could be removed while in the ICU in two cases (Table 6).

The most frequent diagnostic procedures were renal biopsies 5/17 (29.4%), in addition, five abdominal procedures were performed, two emergent cesarean deliveries, one embolization of an arteriovenous fistula, two bronchoalveolar lavages, one pleural decortication, and one femoropopliteal arterial bypass.

Complications and outcomes

Infections occurred in 29 events (64.4%), 20 (69.0%) corresponding to nosocomial infections, of these, pneumonia was the most frequent 12/20 (60.0%). Seven events were community-acquired infections consisting mainly in urinary tract infections which occurred in three patients (42.9%) (Table 7). Of the 29 infectious events in 21 (72.2%), microbiological isolation was obtained with a total of 43 germs, of them there were 24 g negative bacilli (BGN) (55.8%), being the most frequent *E.coli* with five (11.6%) isolates. Twelve of the isolates were gram positive cocci (CGP) (27.9%), with *S.aureus* as the most frequent one with five isolates (11.6%). There were five fungal isolations (11.6%) and two (4.7%) of *Mycobacterium tuberculosis*.

Table 5 Comparison of principals reasons for admission and main variables

	Infection	NO Infection	P value	Disease activity	NO disease activity	P value
Age	30	24.5	0.345	25	32	0.146
Disease diagnosis time in years	2	2	0.972	2	2	0.470
Comorbidities	11	21	0.091	17	15	0.429
Organic basal commitment						
• Renal	16	22	0.641	23	15	0.126
• CNS	4	9	0.257	8	5	0.429
• Pulmonary	4	4	0.456	5	3	0.498
• Hematologic	12	11	0.140	14	9	0.333
APACHE score	16	12	0.007	14	12	0.457
LODS score	7	6	0.199	6	6	0.806
CRP	8.3	3.6	0.011	5.1	4.3	0.585
Previously steroid use	16	21	0.544	21	16	0.513
Organic commitment during hospitalization						
• Renal	9	11	0.486	16	4	0.004
• Pulmonary	7	11	0.477	13	5	0.062
• Hemolytic anemia	7	6	0.250	13	0	0.001
• Thrombocytopenia	7	6	0.250	12	1	0.001
Dyalysis support	6	19	0.438	10	6	0.352
Immunoglobulin use	5	2	0.1	6	1	0.089
Time at ICU	5	4	0.224	3	4.5	0.818

Boldface is the values with stadistic significance $p < 0.05$

Table 6 Therapeutic management during the stay in the ICU

Therapeutic treatment	N = 45 n(%)
Required antibiotic	31 (68,9)
• Carbapenem	15 (33,1)
• Piperacillin / tazobactam	12 (26,7)
• Vancomycin	10 (22,2)
• Ceftriaxone	7 (15,5)
• Ampicillin sulbactam	5 (11,1)
• Anti MRSA does not vancomycin *	5 (11,1)
• Ciprofloxacin	4 (8,9)
• Tuberculosis treatment	3 (6,7)
• Cefazolin	3 (6,7)
• Clarithromycin	2 (4,4)
• Polymyxin B	1 (2,2)
• Penicillin	1 (2,2)
Required Antifungal	7 (15,5)
• Fluconazole	4 (8,9)
• Voriconazole	2 (4,4)
• Caspofungin	1 (2,2)
• Anidulafungin	1 (2,2)
Immunosuppression	
• Pulses Methylprednisolone	22 (48,9)
• Cyclophosphamide	18 (40,0)
• Immunoglobulin	7 (15,5)
• Rituximab	3 (6,7)
Supports	
• Mechanical ventilation	14 (31,1)
• Days, Medium (RIQ)	5,5 (3–17,75)
• Dialytic support	16 (35,5)
• Vasopressor support	9 (20,0)
Procedures	17 (37,7)
Red blood cells transfusion	31 (68,9)
Platelet aferesis	7 (15,5)
Fresh frozen plasma	8 (17,7)
Plasmaferesis	1 (2,2)

* Anti MRSA not vancomycin (Daptomycin, clindamycin and linezolid)

Acute kidney injury was observed in 24 events (53.3%), of these 12/24 (50.0%) KDIGO 3. The LODS score on admission (was available in 38 events) was 6 (RIQ 5–8). The median number of days of mechanical ventilation was 5.5 (RIQ 3–17), the median time of stay in the ICU was four days (RIQ 2–7).

Finally, in terms of mortality, four patients died (12.1%), two of them were men. Three deaths were due to septic shock and subsequent multiple organ failure and the remaining one due to accidental decannulation after tracheostomy with secondary ventilatory failure, all

Table 7 Complications and outcomes

Complications	n/N (%)
Infections	29/45 (64,4)
• Nosocomial	20/29 (69,0)
○ Pneumonia	12/20 (60,0)
○ Urinary tract infection	7/20 (35,0)
○ Bacteriemia	7/20 (35,0)
○ Soft tissue	2/20 (10,0)
○ Intrabdominal	1/20 (5,0)
• Acquired in the community	7/29 (24,1)
○ Urinary tract infection	3/7 (42,9)
○ Pneumonia	2/7 (28,6)
○ Bacteriemia	2/7 (28,6)
○ Soft tissue	1/7 (14,3)
○ Intrabdominal	1/7 (14,3)
• Nosocomial and acquired in community	2/29 (6,9)
Acute kidney injury	24/45 (53,3)
Re-admissions to ICU	7/45 (21,2)
Death	4/33 (12,1)

Boldface is the values with estadistic significance $p < 0.05$

had an infection at the time of death, and three were receiving dialysis support.

Discussion

The present study describes the characteristics of all the admissions to the ICU of patients in a reference center for RD. As expected, there is a predominance of women of reproductive age typical of the behavior of the disease [1, 12, 15]. Compared with different series, both the age and the predominance of the female sex are similar; this is important because although the SLE tends to be thought of as a single entity, its behavior varies significantly according to sex, race, and age [16]. This is evidenced, for example, in Abramovich's study [17] that evaluated the mortality of patients with SLE who were admitted to the ICU due to sepsis. In this study, the average age of admission was 55 years with an accumulated damage scale in SLICC lupus [18, 19] between 5 and 7, which is a high value and with cardiovascular comorbidity in 27%. The mortality found was 31%, with the main risk factor being cardiovascular dysfunction due to sepsis, a finding that is not found in other series and was expected considering their baseline characteristics.

Despite the young age of the patients, it was found a high rate of comorbidities, especially high blood pressure, which was present in 42% and renal failure with 18%, these being unusual in such a high proportion in this age group and making more difficult the management of these patients [3, 8]. Interestingly, patients entered with high levels of disease activity (SLEDAI 20) but with an APACHE median score of 13, which is low

compared to other series of both rheumatologic diseases in general [2, 8, 20] as well as those that consider SLE only [1, 4, 16, 21–24]. This aspect is important given that mortality in this study is one of the lowest reported even though the SLEDAI score was elevated whether it is compared with the oldest series (40%) [1, 16, 24] or with the most recent ones, where mortality is around 20% [23, 25]. A possible explanation for this finding is the low APACHE score of these patients reflecting an early admission strategy to the ICU.

The leading cause of admission was activity; this differs from several series, where infection plays a preponderant role [1, 21, 23]. Only a few cohorts report disease activity as a cause of hospitalization [25, 26] and in some, as in the study by Whitelaw et al. [27] more than half of the patients had less than six months of diagnosis of SLE, which would explain the predominance of activity. In the present cohort, the average time of diagnosis was two years; the high activity was possibly a reflection of difficulties in outpatient management. This should be highlighted given that reduced access to health services has been associated with a worse prognosis in SLE [28] and is usually associated with the requirement of greater immunosuppressive therapy for more extended periods and consequently greater cumulative damage. When comparisons were made between patients with infections as a reason for admission to ICU, it was found that APACHE was higher, as well as the CRP. Also, in patients with activity of disease at baseline was more common renal involvement, hemolytic anemia, and thrombocytopenia. However, it should be noted that this analysis is merely exploratory and should be verified with other types of studies. In addition, the cause of infection with disease activity was sometimes overlapped, given the difficulties that often exist in differentiating one from the other and that the same infection can lead to disease activity.

Infections were nosocomial in 69%, which explains the broad antimicrobial spectrum used. There was a large amount of gram-negative bacillus being *E.coli* the leading isolation, nonetheless, there were other germs that are not common in the non-immunosuppressed population as previously reported [1, 28]. This high percentage of infection can be explained by the high number of patients in whom a high dose of methylprednisolone treatment was required to control the activity of the disease. Previous studies have shown that the use of steroids is an independent risk factor for infection [4, 28].

Mechanical ventilation was used in 31% of the patients for a median of 5 days, which is lower than that reported in other cohorts, where it was used between 68 and 77% of patients for an average of 10 days [7, 9, 20, 29]. This may be due to the cause of admission in our patients in which renal involvement predominated. This could be one of the reasons for the overall low mortality, and

possibly reflects the transfer of less ill patients to the ICU as evidenced by its APACHE score as has been mentioned previously.

The median of LODS score was 6 and of APACHE II score was 13, which predicts mortality of 18.6%, higher than the observed. Concerning the APACHE II score, some series have shown their correlation with mortality, although in most of them with confidence intervals close to unity [9, 22, 30]. The mean value of APACHE II in this study was low if the series mentioned above are considered, even more, when the predictive value found in several studies is between 18 and 20 [9, 22, 30].

One aspect that is worth mentioning is that all cases of mortality were related to infectious processes; which emphasizes the need to perform subsequent analyzes in order to detect factors that may be modifiable. Finally, it is striking that half of the patients who died were men, which is in agreement with the prognosis that has been established, where sex has a significant weight in manifestations and mortality [31–33].

This study has several limitations, due to its retrospective nature it was frequent that the medical records lacked some data. On the other hand, having been performed in a single center of the third level of complexity may limit the applicability of these findings.

Conclusions

In this cohort, it was the activity of the disease and not infectious complications the main reason for admittance to the ICU. This may be due to difficulties in monitoring and continuity of treatments, which makes relapse more frequent and immunosuppression more aggressive. Mortality was low, but it occurred more frequently in patients with infections, especially of nosocomial origin. Given these characteristics of the population, it is necessary to improve the conditions of access to health and generate more strict protocols in the ICU to avoid infections.

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Authors' contributions

All authors contributed equally in the design of the study, collection, analysis of the data and in the writing of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

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

Ethics approval and consent to participate

This research was approved by the UPB Health Research Ethics Committee and the authorization by the CUB for access to patient records.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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