UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO

FACULTAD DE MEDICINA

LUPUS PATIENTS IN AN EMERGENCY UNIT. CAUSES OF CONSULTATION, HOSPITALIZATION AND OUTCOME. A COHOT STUDY

TESIS

QUE PARA OBTENER EL TÍTULO DE:

ESPECIALISTA EN MEDICINA INTERNA

PRESENTA:

ROJAS SERRANO, JORGE

ASESOR: CARDIEL RIOS, MARIO HUMBERTO

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ASUNTO: Autorización del trabajo de investigación del Dr. Jorge Rojas Serrano.

DR. ISIDRO AVILA MARTINEZ
SECRETARIO DE SERVICIOS ESCOLARES
DE LA FACULTAD DE MEDICINA
Presente.

Estimado Dr. Avila Martínez:

Me permito informar a usted que el **Dr. Jorge Rojas Serrano**, alumno del curso de especialización en **Medicina Interna** en el **Instituto Nacional de Ciencias Médicas y de la Nutrición "Dr. Salvador Zubirán"**, presenta el trabajo de investigación intitulado ***"Lupus patients in an emergency unit. Causes of consultation, hospitalization and outcome. A cohort study".***

De conformidad con el artículo 21 capítulo 5º. de las Normas Operativas del Plan Unico de Especializaciones Médicas (PUEM) se considera que cumple con los requisitos para validarlo como el trabajo formal de Investigación que le otorga el derecho de la diplomación como especialista.

Sin otro particular de momento, reciba un cordial saludo.

Atentamente
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PAPER

Lupus patients in an emergency unit. Causes of consultation, hospitalization and outcome. A cohort study

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The objectives were to determine causes of consultation, hospitalization and outcome in a cohort of lupus patients in an emergency unit.

Patients with systemic lupus erythematosus (SLE) who visited the emergency department for consultation from 1 September 1996 to 17 May 1997 were included in the study. They were evaluated during the visit by looking at 100 variables such as demographic, socioeconomic, clinical, therapeutical, behavioral, (compliance), emotional (Beck depression inventory), disease activity, (Mex-SLEDAI), disease severity (Lupus SDI), chronic damage (SLICC-ACR), and physician's and patient's global assessments of severity. All causes of consultation, hospitalization and outcome were registered. Descriptive statistics, univariate analysis and multiple logistic regression were used for analysis. Significance was set at the 0.05 level.

180 patients were included. 164 were female, mean age 31.7/11.39 y, mean Mex SLEDAI score 3.8, mean SLICC-ACR 1.3. Fever, poliarthralgia and abdominal pain were the main causes of consultation with 26, 25 and 18 cases each. 49 patients were hospitalized and these were statistically different than non-hospitalized patients in level of formal education (10.2 *vs* 11.8, $P = 0.03$); compliance (7.6 *vs* 9, $P = 0.0001$); malar rash (57% *vs* 82%, OR, 95% CI = 0.28, 0.13–0.62, $P = 0.0008$), chloroquine daily dose intake (45 *vs* 77 mg, $P = 0.04$); disease severity in physician's global assessments (5.6 *vs* 2.1, $P = 0.0001$) and Beck depression inventory (21 *vs* 16, $P = 0.01$). Multiple logistic regression identified physician's global assessment, fewer ACR criteria and higher SLICC-ACR scores as the main variables associated with hospitalization. Five patients died; two with community acquired pneumonia, one with pancreatitis, multiple thromboses, and sepsis, one with pulmonary hemorrhage; and one with pulmonary thromboembolism.

In conclusion, poor compliance, low level of formal education, severity, depression, lower ACR criteria and higher SLICC-ACR scores were important variables identified with hospitalization. Chloroquine use seemed to have a protective effect. Causes of death were related to infections and antiphospholipid syndrome. *Lupus* (2000) **9**, 601–606.

Keywords: systemic lupus erythematosus; emergency medicine; compliance; depression

Introduction

Although the prognosis of systemic lupus erythematosus (SLE) has improved, these patients may develop severe disease activity, serious side effects,[1] infections,[2–4] antiphospholipid syndrome[5] and organ involvement, all of them related with bad outcomes. Although general causes of hospitalization have been defined,[6] causes of consultation and hospitalization of lupus patients attending an emergency unit have not. The aim of this study was to determine causes of consultation, hospitalization and outcome in a cohort of lupus patients seen in a tertiary care center and identify modifiable psychosocial factors related to poor outcome.

Material and methods

Patients

All patients with at least four of the American Rheumatism Association classification criteria[7] who

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visited the emergency unit for consultation at the Instituto Nacional de Ciencias Medicas y Nutrición, Salvador Zubirán from September 1996 to May 1997 were invited to participate. We excluded repeated visits. The Institutional Review Board approved the proposal and patients gave written informed consent to participate.

Clinical evaluation

All patients answered questions about their age, social status, and demographic variables. These included level of formal education, socioeconomic status using a local classification, family monthly income, number of people living at patient's home, age at first symptom, age at diagnosis, compliance with medical appointments, drug intake and laboratory assessments, these compliance variables being scored on a 0 (none) to 10 (excellent) scale. We also registered regular use of alcohol, tobacco, or illicit drugs. This information was validated with medical records. The main cause of consultation was registered. Patients were asked to fill out validated Spanish versions of the Beck depression inventory (BDI),[8] and the Arthritis Impact Measurements Subscales for depression (AIMSD) and anxiety (AIMSA).[9] In cases where the patient could not provide this information, it was considered as a missing value only for these variables. Medical treatment was registered and annual total dose was calculated for the following drugs: prednisone, chloroquine, azathioprine, methotrexate and cyclophosphamide. We filled out the MEX-SLEDAI index,[10] the lupus severity disease index[11] (lupus SDI) and the Systemic Lupus Erythematosus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus[12] (SLICC-ACR) by physical examination and laboratory assessment to measure disease activity, severity and chronic damage, respectively. The antiphospholipid syndrome (APS) was defined by a history of arterial or venous thromboses, recurrent fetal losses, thrombocytopenia, and abnormal high titers of antiphospholipid antibodies.[13] Each patient was asked to qualify severity using visual analogue scales (0 to 10, with 0 no severity to 10 highest severity level). Physician's global assessments of severity and activity of SLE using visual analogue scales (0 to 10, 0 no severity/activity, 10 highest level of severity/activity) were also obtained. All discharge diagnoses were registered, and in the case of hospitalization, all patients were followed until their final outcome was obtained.

Statistical analysis

Only first visits were analyzed. Descriptive and inferential statistics were applied as appropriate. Comparisons among hospitalized versus non-hospitalized patients with non-parametric and parametric statistics were made. Stepwise multiple logistic regression was used to evaluate participation of independent variables associated with hospitalization. Significance was set at the 0.05 level.

Results

183 SLE patients went to the emergency unit for medical consultation, all except three being accepted to participate in the study. The mean age was 32 ± 11.3 (range 14–77) y, with 164 (91.1%) female and 16 (8.9%) male. 38 (21.1%) patients had APS. The main cause of consultation was fever in 26 (14.4%) patients, followed by arthralgias, abdominal pain, airway symptoms and chest pain with 25 (13.8%), 18 (9.9%), 14 (7.7%) and 11 (6.1%) patients, respectively (Figure 1). 40% of patients were of a low socioeconomic status. Family monthly income had a mean of 2448 ± 2377 (range 0–14,000) pesos, or 259 ± 251 (range 0–1481.4) US dollars. Mean formal education was 11.3 ± 4.37 (range 0–21) y. Mean age of first SLE symptom was 23.4 ± 10 (range 4–64) y, with a mean age of SLE diagnosis 25.6 ± 10.2 (range 11–64) y. Compliance with office visits had a mean of 8.6 ± 2.2 for every ten planned appointments, compliance with drug prescription had a mean of 8.3 ± 2.2 for every 10 pills the patient had to take, and compliance with laboratory assessments had a mean of 8.9 ± 2.1 for every ten appointments. The mean prednisone daily dose was 10.9 ± 15.9 (range 0–75) mg and the mean of prednisone total dose in the last year was 3141.4 ± 3584.2 (range 0–18,200) mg. The mean azathioprine daily dose intake was 22.7 ± 41.2 (range 0–150) mg. The mean annual azathioprine total dose intake in the last year was $8039 \pm 15,182$ (range 0–59,400) mg. Chloroquine mean daily dose intake was 68.6 ± 93 (range 0–300) mg. Chloroquine mean total dose intake in the last year was $19,264 \pm 27,400$ (range 0–98,150) mg. The mean value of the MEX-SLEDAI index was 3.8 ± 4.5 (range 0–17). The mean value of the SLICC/ACR was 1.3 ± 1.7 (range 0–9). Lupus SDI index mean was 4.8 ± 2.3 (range 1–12). Beck depression inventory had a mean of 17.9 ± 11.1 (range 0–46). The AIMSD and AIMSA had means of 3.3 ± 1.1 (range 0–6.6) and 3.59 ± 1.2 (range 0–6.3) respectively. Patient's perception of severity had

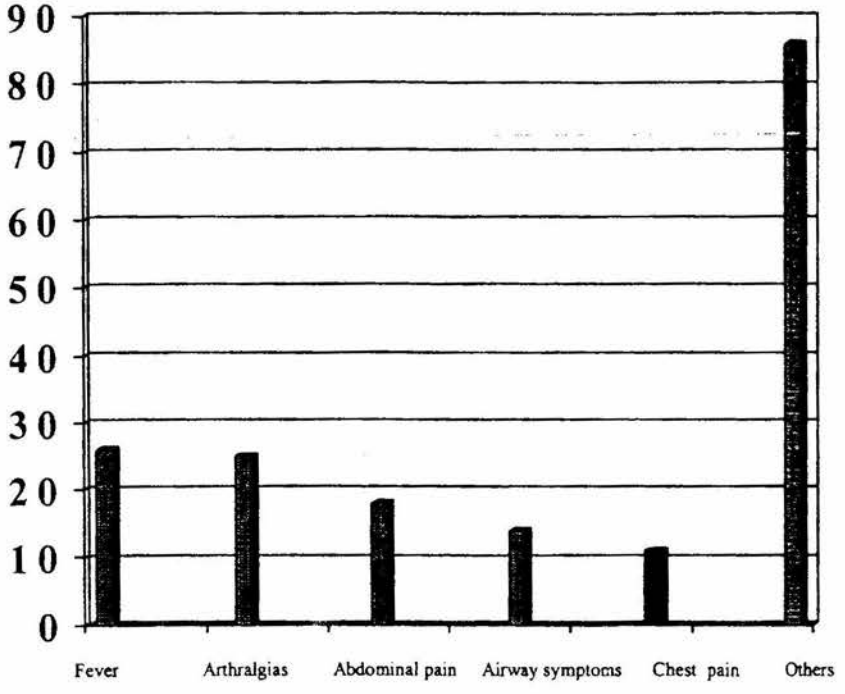

Figure 1 Most common causes of consultation in 180 SLE patients.

mean of 5.38±3.0. Physician's global assessment of severity and SLE activity had a mean of 3.09±4.3 and 3.3±4.3, respectively. 131 (72.8%) patients were discharged from the emergency unit, while 49 (27.2%) patients were hospitalized.

Discharged patients

Of these patients, 120 (91.6%) were female and 11 (8.4%) male, and 23 (17.6%) patients had APS. Mean age was 31.2±10.1 y (range 14–77 y). Education had a mean of 11.8±4.3 (range 0–21) y of formal education. The family monthly income had a mean of 2482±2465.3 (range 0–14,000) pesos or 262.6±260.8 (range 0–1481.4) US dollars. Compliance with office visits had a mean of 9.02±1.7 of every ten appointments. Compliance with drug prescription was 8.6±1.8 for every ten pills the patient had to take. Compliance with laboratory assessments was 9.2±1.7 for every ten appointments. MEX-SLEDAI index was 3.5±4.3 (range 0–17). The SLICC/ACR and the lupus SDI indices had a mean of 1.2±1.7 (range 0–9) and 4.7±2.4 (range 1–12), respectively. The mean Beck depression inventory was 16.7±10.2 (range 0–46). The patient's perception of severity had a mean of 5.1±3. The physician's global assessment of severity had a mean of 2.1±2.2. The following were the main causes of consultation in this group: fever in 16 (12%); upper airway symptoms in 14 (10.7%); abdominal pain in 9 (6.9%) patients. The main discharge diagnosis were infections in 35 (26.7%) patients (urinary tract infections in 14; 12 had upper airway infections, 9 had acute diarrhea). SLE disease activity in 24 (18.3%) patients, and 9 (5%) patients had their SLE diagnosis made in this visit (Figure 2).

Hospitalized patients

49 (37.4%) patients were hospitalized. 5 (10.2%) patients were male, while 44 (89.8%) patients were female. 15 (30.6%) patients had APS. The mean age was 33±14.2 (range 15–68) y. Education had a mean of 10.2±4.4 (range 1–17) y of formal education. The family monthly income had a mean of 2358.9±2146 (range 300–10,000) pesos or 249.6±227 (range 31.7–1058.2) US dollars. Compliance with office visits had a mean of 7.5±2.7 of every ten appointments. Compliance with drug prescription was 7.4±2.8 for every ten pills. Compliance with laboratory assessments had a mean of 7.4±2.8 for every ten appointments. MEX-SLEDAI index was 4.6±5 (range 0–17). The lupus SDI and SLICC/ACR had a mean of 5±2.1 (range 1–11) and 1.7±1.7 (range 0–8) respectively. The patient's perception of severity had a mean of 6±3. The mean of the physician's perception of global assessment of severity was 5.6±2.6. The main causes of

consultation in this group were fever in 10 (20.4%); abdominal pain in 8 (16.3%); dyspnea in 6 (12.2%) and arthralgias in 5 (10.2%) patients. The main diagnosis for hospitalization was first time SLE diagnosis in 6 patients (12.2%), and acute abdomen in 6 patients (12.2%), with SLE disease activity in 3 patients (6.1%), deep venous thromboses, neutropenia and fever, and bacterial spontaneous bacterial peritonitis with 2 (4%) patients each. The mean hospitalization stay was 10.9 ± 8.8 d (range 0–41 d). The main discharge diagnoses were 14 (28.5%) patients with diverse infectious diseases; 6 (12.2%) patients with SLE diagnosis for the first time and 6 (12.2%) patients with SLE activity. 5 (10.2%) patients died; 2 due to community acquired pneumonia, 1 with pulmonary embolism, 1 with pulmonary hemorrhage, and 1 with acute pancreatitis, multiple thromboses and sepsis (Table 1).

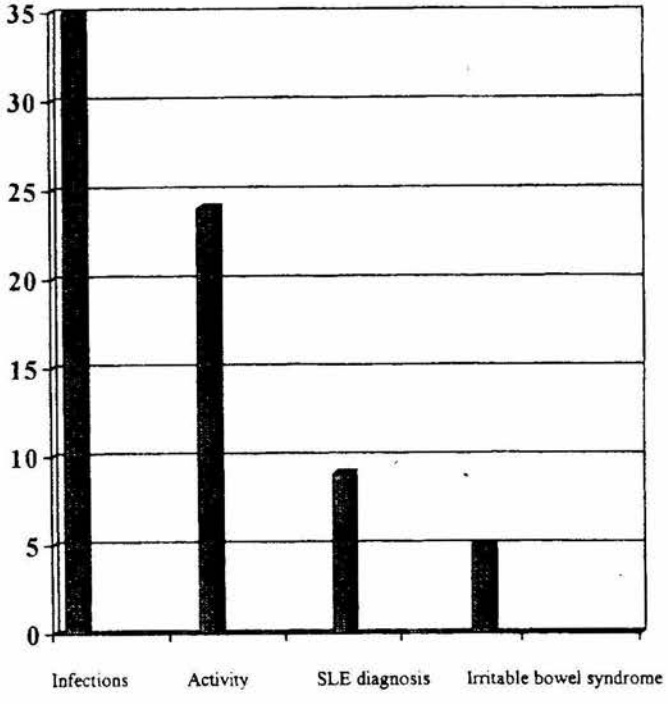

Figure 2 Most common discharge diagnoses in 131 SLE patients.

Table 1 Differences between hospitalized versus non-hospitalized, SLE patients

	Hospitalized	*Non-hospitalized*	*P value**
n (%)	49 (37.4)	131 (62.6)	
Education (y) (μ, δ)	10, 4	12, 4	$P=0.03$
Compliance (0–10) (μ, δ)			
(a) Office visits	7.6, 2.7	9, 1.8	$P=0.0001$
(b) Drugs	7.4, 2.8	8.6, 1.8	$P=0.002$
(c) Laboratory	8, 2.6	9.2, 1.7	$P=0.001$
Depression (BDI) (μ, δ min, max)	21, 3	16.7, 10.2	$P=0.0001$
Physician's global assessment (0–10) (μ, δ)	5.6, 2.6	2.1, 2.2	$P=0.0001$
Chloroquine daily dose (mg) (μ, δ)	45, 85	77, 94	$P=0.04$
Chloroquine last year total dose (mg) (μ, δ)	11,341, 21,863	22,228, 28,718	$P=0.0008$
Malar rash (%)	57	82	$P=0.008$
Photosensivity (%)	69.3	87	$P=0.01$
ACR criteria (μ, δ)	6.5, 1.3	7.2, 1.7	$P=0.005$

*Significance according to chi square or unpaired *t*-tests.

Comparison between hospitalized versus non-hospitalized patients

Hospitalized (49 cases) patients differed from non-hospitalized patients (131 controls) in years of formal education with 10.2 ± 4.4 *vs* 11.8 ± 4.2 ($P=0.03$). Non-hospitalized patients had better compliance with office visits: 9 ± 1.8 *vs* 7.6 ± 2.7 ($P=0.0001$); medications, 8.6 ± 1.8 *vs* 7.4 ± 2.8 ($P=0.002$) and laboratory assessments with 9.2 ± 1.7 *vs* 8 ± 2.6 ($P=0.001$). Non-hospitalized patients had lower scores in the Beck depression inventory with 16.7 ± 10.2 *vs* 21 ± 3.04 ($P=0.01$). Physician's global assessment of severity was lower in non-hospitalized patients, 2.1 ± 2.2 *vs* 5.6 ± 2.6 ($P=0.0001$). The number of ACR criteria was lower in hospitalized patients (6.5 ± 1.3 *vs* 7.2 ± 1.5; $P=0.005$). Hospitalized patients were taking lower doses of chloroquine 45 ± 84.9 *vs* 77 ± 94 mg/d ($P=0.04$) and they also had lower annual total dose of chloroquine $11{,}341.8 \pm 21{,}863.8$ *vs* $22{,}228.2 \pm 28{,}718$ mg ($P=0.01$). No differences were found with other drugs. Malar rash was more prevalent in non-hospitalized patients (82% *vs* 57%; odds ratio, 95% CI 0.28, 0.13–0.62 ($P=0.0008$). Photosensitivity was also more prevalent in the non-hospitalized group (87% *vs* 69.3%; odds ratio, 95% CI 0.34, 0.14–0.8 $P=0.01$) (Table 2).

Stepwise multiple logistic regression identified three variables associated with hospitalization. Physician's global assessment of disease severity was the most important variable ($P=0.00001$), accounting for 25.8% of the log likelihood. Fewer ACR criteria were also associated with hospitalization ($P=0.00$ as

Table 2 Causes of death of hospitalized patients

Community acquired pneumonia	2
Pulmonary hemorrhage	1
Pulmonary embolism	1
Pancreatitis, multiple thromboses, sepsis	1
Total	5

well as higher SLICC-ACR scores ($P = 0.01$). The model had a P value of 0.00001 and accounted for 34.3% of the log likelihood.

Weak but statistically significant Spearman's rank correlations were found between Beck depression inventory and physician's global assessment of severity ($rs = 0.18$); disease activity ($rs = 0.17$); formal education ($rs = -0.24$); family income ($rs = -0.19$) and prednisone intake ($rs = 0.16$).

Discussion

The main cause of consultation in this cohort was fever, and the main discharge diagnosis was infection. The second discharge diagnosis of both hospitalized and non-hospitalized patients was disease activity. This is important since the main cause of hospitalization in the Hopkins Lupus Cohort[6] was disease activity (35%), with infection and/or active SLE being the second most likely cause (14%). This different proportion and order of causes is something that can be explained by different populations and socioeconomic characteristics between settings. Fever is a main cause of consultation and hospitalization, it has special difficulties to differentiate between SLE activity and infection, and some patients may have both, as it was represented in some of the 14% of cases in the Johns Hopkins study.[6] Infections were the main cause of death in SLE patients[1, 14] and there are multiple reports of uncommon infections in this group of patients.[2–4, 15] This was also the case in this cohort. These findings support the concept that clinicians should look carefully for infectious in every SLE patient with fever.

It is interesting to notice that some variables associated with hospitalization in this cohort were socioeconomic and behavioral rather than disease oriented, such as level of formal education, compliance, and depression. Both low level of education[16] and depression[17] have been related to bad outcomes. Depression could affect patients' behaviour in multiple ways. Compliance is a good example, since a depressed patient is probably more likely to stop taking lupus treatments, they tend to avoid their usual clinical appointments and these could be related with poor disease control, all of which will decrease self-efficacy. These are potentially modifiable factors with early identification, proper education and adequate counseling.

Similar findings with low level of formal education have been detected in our setting with rheumatoid arthritis patients.[18] Depression in SLE was associated with disability in a study done by Ward *et al.*[19] They also identified disease activity with less social support and organ damage with lower self-esteem and time orientation favoring the present over the future. Karlson *et al*[20] identified that higher education, private insurance/Medicare and higher income were associated with less disease activity at diagnosis but these were unstable measures. Another study by Karlson *et al*[21] found that disease activity was most strongly associated with lower self-efficacy, less social support and younger age. Lower self-efficacy was associated with worse physical function. Social support was also associated with better physical, social and emotional variables in a study conducted by Sutcliffe *et al.*[22]

Physician's global assessment of severity was greater in the hospitalized group. This was expected and is the most important variable identified in a stepwise multiple logistic regression model. This is not a surprise since it is the physician who decides if the patient has to be hospitalized.

15 patients were discharged with a diagnosis of SLE. Our institution is a referral center for SLE and related diseases, which is a possible explanation of this finding. We did not find trauma as a major cause of consultation, nor obstetrical causes. Our institution does not provide these services as a main part of their attention. There are other specialized institutions that take care of these specific problems.

Chloroquine intake seemed to have a protective effect, as did malar rash and photosensitivity. Chloroquine has been found as a protector against mortality.[23] The possible explanation is that chloroquine is used to treat mucocutaneus SLE and this is reflecting lower SLE disease activity and severity. Nevertheless another explanation is possible through a pharmacologic long-term clinical benefit, since consistent information regarding antimalarials intake as a protective factor against SLE relapses is available in two studies from the same Canadian group.[24,25] They have shown in a randomized controlled study that the relative risk to develop a flare-up was 2.5 times higher in SLE patients who stop taking hydroxichloroquine. They also found that the relative risk of a severe exacerbation of disease was 6.1 time higher for the patients taking placebo. Mortality in this cohort was related to infections, SLE activity and the AFS. In summary, poor compliance with medical treatment, low level of formal education, physician's global assessment of severity and depression were important variables identified with hospitalization. Chloroquine use and skin involment seemed to have a protective effect. The main diagnoses at discharge were infections and disease activity, and causes of death were related to infections and the antiphospholipid syndrome.

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