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Systemic lupus erythematosus: Pharmacological differences between women and men and among age groups and geographical regions

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ABSTRACT

Systemic lupus erythematosus (SLE) is a chronic and potentially fatal autoimmune disease. There are clinical differences between women and men and among age groups. Its treatment involves a heterogeneous group of drugs. The objective was to determine the pharmacological treatment patterns in a group of patients with SLE and compare them according to sex, age group and geographic region. This was a cross-sectional study that identified outpatient drugs used in patients with SLE from a population database of Colombians affiliated with the Colombian Health System. Sociodemographic and pharmacological variables were considered. Descriptive and bivariate analyses were performed. A total of 4307 patients with SLE were identified (median age, 44.2 years; 89.4% women). Disease-modifying antirheumatics were the most prescribed drugs (90.5%), especially chloroquine (54.4%), which predominated in all age groups and geographical regions. Hydroxychloroquine and methotrexate were the predominant prescribed drugs for women, while corticosteroids, chloroquine, azathioprine, and mycophenolate were the predominant prescribed drugs for men. The use of corticosteroids (prednisolone and prednisone) decreased with increasing age. Differences were found in the prescription of drugs for patients with SLE between women and men and among geographic regions and age groups. The use of chloroquine predominated over hydroxychloroquine, contrasting with clinical practice guidelines.

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Lupus eritematoso sistémico: diferencias farmacológicas entre mujeres y hombres, grupos de edad y regiones geográficas

Palabras clave:
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RESUMEN

El lupus eritematoso sistémico (LES) es una enfermedad autoinmune crónica y potencialmente mortal. Existen diferencias clínicas entre mujeres y hombres, y entre grupos de edad. Su tratamiento involucra un grupo heterogéneo de medicamentos. El objetivo fue determinar los patrones de tratamiento farmacológico de un grupo de pacientes con LES y compararlos según el sexo, los grupos de edad y las regiones geográficas. Estudio de corte transversal que identificó los medicamentos de uso ambulatorio empleados en pacientes con LES, a partir de una base de datos poblacional de colombianos afiliados al Sistema de Salud de Colombia. Se consideraron variables sociodemográficas y farmacológicas. Se realizó un análisis descriptivo y bivariado. Se identificó a 4.307 pacientes con LES, con una mediana de edad 44,2 años y un 89,4% mujeres. Los medicamentos modificadores de enfermedad reumática fueron los más prescritos (90,5%), en especial cloroquina (54,4%), el cual predominó en todos los grupos de edad y las regiones geográficas. La hidroxicloroquina y el metotrexato predominaron en mujeres, mientras que los corticosteroides, la cloroquina, la azatioprina y el micofenolato, en hombres. Con el aumento de la edad disminuyó el uso de corticoides (prednisolona y prednisona). Se encontraron diferencias en la prescripción de los medicamentos empleados en los pacientes con LES entre mujeres y hombres, regiones geográficas y grupos etarios. El uso de cloroquina predominó sobre la hidroxicloroquina, en contraste con lo recomendado por las guías de práctica clínica.

Introduction

Systemic lupus erythematosus (SLE) is a chronic and life-threatening autoimmune disease that can affect any organ, such as the skin, kidneys, joints, central nervous system and cardiovascular system.[1] Its global prevalence has been estimated at 9–241 per 100,000 person-years, with an incidence of 0.3–23.2 per 100,000 person-years, ranging from 2.4 to 7.4 in Europe to 7.9 in Central and South America and 8.1 in Asia.[2] It is more common in women, with a ratio of women to men of 7–15:1 for adults and 3–5:1 for pediatric patients.[2] However, in the latter group and in men, SLE appears to be much more aggressive, with a greater presence of clinical manifestations and higher severity.[3,4]

In Colombia, between 2012 and 2016, 431,834 cases of SLE were identified, with an unadjusted prevalence of 91.9 cases per 100,000 inhabitants; in those over 18 years of age, the prevalence was 126.3 per 100,000 inhabitants.[5] There is evidence of greater aggressiveness in the clinical presentation of SLE in men, who present with greater lung involvement, longer hospital stays and high readmission and lethality rates.[6]

In the pharmacological treatment of SLE, antimalarials, corticosteroids, immunosuppressants and biotech drugs stand out; these drugs are used to induce remission or reduce disease activity and prevent flare-ups and target organ damage.[7] Management is individualized and must take into account the clinical manifestations, complications, severity and degree of disease activity.[7–9] However, these drugs are not innocuous and may be associated with adverse reactions, such as increased susceptibility to infections, increased risk of cardiovascular diseases, diabetes and cancer, and decreased bone density.[1,10]

The existing information on the prescription patterns of drugs used in rheumatological diseases is scarce in Colombia, and an understanding of these patterns can help direct informed interventions that focus on the appropriate use of these drugs. Such prescription patterns vary among countries and may also differ among their different regions; therefore, we sought to determine the pharmacological management of patients with SLE and to identify the differences between women and men and among age groups and geographical regions in Colombia.

Materials and methods

This was a cross-sectional study on the prescription patterns of drugs used for patients diagnosed with SLE; the data were obtained from a population database for drug dispensing that collects information from approximately 8.5 million people affiliated with the Colombian Health System in six health insurance companies, corresponding to approximately 30.0% of the active population covered by the contributory or paid regime and 6.0% covered by the state-subsidized regime, which together comprise 17.3% of the Colombian population.

Patients were identified using International Classification of Diseases (ICD-10) codes related to SLE (M321, M328, M329) in the period from July 1, 2019, to June 30, 2020. Patients of any age and sex who were seen as outpatients and were under pharmacological management for SLE were selected. Patients with

a concomitant diagnosis of cutaneous lupus erythematosus or drug-induced lupus and those diagnosed with SLE without pharmacological treatment were excluded.

Based on the information on the prescription of drugs to the affiliated population, systematically obtained by a dispensing company (Audifarma SA), a database was designed that allowed the collection of the following groups of patient variables:

1. Sociodemographic: sex, age (groups: <20 years, 20–39 years, 40–64 years and ≥65 years), health system regime affiliation (contributory or subsidized) and city of dispensation;
   - Geographical areas: The place of residence was categorized by department according to the regions of Colombia and considering the classification of the National Administrative Department of Statistics (DANE) of Colombia, as follows:
   - Caribbean region: Atlántico, Bolívar, Cesar, Córdoba, La Guajira, Magdalena, Sucre, San Andrés, Providencia and Santa Catalina.
   - Central region: Antioquia, Caldas, Quindío, Risaralda, Caquetá, Huila and Tolima.
   - Bogotá-Cundinamarca region.
   - Eastern region: Boyacá, Meta, Norte de Santander, Santander, Arauca and Casanare.
   - Pacific region: Cauca, Chocó, Nariño, Valle del Cauca, and
   - Amazon-Orinoco Region: Amazonas, Guaviare, Guainía, Vaupés, Vichada and Putumayo.
2. Drugs for SLE management:
   - Corticosteroids: prednisolone, prednisone, deflazacort, and methylprednisolone;
   - Synthetic disease-modifying antirheumatic drugs (DMARDs): methotrexate, azathioprine, leflunomide, chloroquine, hydroxychloroquine, and sulfasalazine;
   - Immunosuppressants: cyclophosphamide, cyclosporine, mycophenolate, and tacrolimus; and
   - Biologic disease-modifying antirheumatic drugs (DMARDb): rituximab, belimumab, and adalimumab; and
3. Comedications (grouped into the following categories): (a) antidiabetics (oral and subcutaneous), (b) antihypertensives and diuretics, (c) lipid-lowering drugs; (d) antiulcers, (e) antidepressants, (f) anxiolytics and hypnotics (benzodiazepines and Z-drugs), (g) thyroid hormone, (h) antipsychotics (typical and atypical), (i) antiepileptics, (j) antiarrhythmics, (k) antihistamines, (l) antidementia drugs, (m) opioid analgesics, (n) nonopioid analgesics, (o) bronchodilators and inhaled corticosteroids, (p) antiplatelet agents, (q) anticoagulants (oral and parenteral), (r) antipsychotics, and (s) hormonal contraceptives.
4. Comorbidities: The main cardiovascular, endocrine, rheumatic, urological, kidney, psychiatric, neurological, digestive, respiratory and neoplastic diseases were identified from the reported ICD-10 diagnostic codes. Autoimmune rheumatological diseases (rheumatoid arthritis, Sjogren's syndrome, vasculitis, polymyalgia rheumatica, psoriatic arthritis, ankylosing spondylitis and systemic sclerosis) and non-immune diseases (fibromyalgia, osteoatrosis, osteoporosis and gout) were included.

Ethical considerations

The protocol was approved by the Bioethics Committee of Universidad Tecnológica de Pereira in the "research without risk" category (approval number: 02-051020). The principles established by the Declaration of Helsinki were respected.

The data were analyzed with the statistical package SPSS Statistics, version 26.0 for Windows (IBM, USA). A descriptive analysis was performed; qualitative variables are presented as frequencies and proportions, and quantitative variables are presented as measures of central tendency and dispersion, depending on the normality of the data, as established by the Kolmogorov–Smirnov test. Quantitative variables were compared using Student's *t*-test or the Mann–Whitney *U* test, and categorical variables were compared using the X^2 test or Fisher's exact test. A statistical significance level of $p < 0.05$ was adopted.

Results

A total of 4307 patients with a diagnosis of SLE were identified, distributed in 135 different cities or municipalities. Of these, 89.4% ($n = 3851$) were women, and the median age was 44.2 years (interquartile range: 32.4–55.8 years; range:6.7–90.8 years); the age group distributions were as follows: <20 years ($n = 198$; 4.6%), 20–39 years ($n = 1560$; 36.2%), 40–64 years ($n = 2120$; 49.2%) and ≥65 years ($n = 429$; 10.0%). Most patients lived in the Bogotá-Cundinamarca Region ($n = 1491$; 34.6%), followed by the Caribbean Region ($n = 1036$; 24.1%), Central Region ($n = 878$; 20.4%), Pacific Region ($n = 753$; 17.5%), and Eastern Region and Amazonia ($n = 149$; 3.5%). A total of 91.2% ($n = 3926$) of the patients participated in the contributory regime, and 8.8% ($n = 381$) belonged to the subsidized regime.

Most patients with SLE were treated with DMARDs ($n = 3901$; 90.5%), with a predominance of chloroquine ($n = 2343$; 54.4%), azathioprine ($n = 1579$; 36.6%), hydroxychloroquine ($n = 1267$; 29.4%) and methotrexate ($n = 758$; 17.6%). Corticosteroids, especially prednisolone ($n = 2915$; 67.6%), were prescribed to 76.1% ($n = 3278$) of patients; among immunosuppressants, mycophenolate was the most prescribed ($n = 719$; 16.7%). The cyclophosphamide was prescribed to 36 patients (0.8%) while DMARDb were prescribed to 11 patients (0.3%).

A total of 71.4% ($n = 3076$) of all patients had some chronic disease. Of these, 67.8% ($n = 2084$) had one or two diseases, 23.6% ($n = 726$) had three or four diseases, and 8.6% ($n = 266$) had five or more diseases. The 10 most common comorbidities were hypertension ($n = 2012$; 46.7%), rheumatoid arthritis ($n = 532$; 12.4%), hypothyroidism ($n = 513$; 11.9%), Sjögren's syndrome ($n = 489$; 11.4%); diabetes ($n = 383$; 8.9%); chronic kidney disease ($n = 277$; 6.4%); depressive disorders ($n = 226$; 5.2%); chronic pain ($n = 207$; 4.8%); anxiety disorders ($n = 179$; 4.2%) and fibromyalgia ($n = 157$; 3.6%). Polyautoimmunity (systemic lupus erythematosus and rheumatoid arthritis and Sjogren's syndrome) occurred in 21.6% ($n = 932$) of patients. In addition, of all patients, 2.7% ($n = 115$) had a diagnosis related to thrombosis. A total of 18.4% ($n = 792$) of the

patients had an infection-related diagnosis, including urinary tract infection ($n = 189$; 4.4%), tuberculosis ($n = 47$; 1.1%), pneumonia ($n = 39$; 0.9%), meningitis ($n = 7$; 0.2%) and sepsis ($n = 7$; 0.2%).

The most common comedications were nonopioid analgesics ($n = 2854$; 66.3%), followed by antiulcers ($n = 2391$; 55.5%), antihypertensives and diuretics ($n = 2234$; 51.9%), antiplatelet agents ($n = 1210$; 28.1%), lipid-lowering drugs ($n = 1078$; 25.0); antidepressants ($n = 1017$; 23.5%), antihistamines ($n = 1002$; 23.3%), opioid analgesics ($n = 949$; 22.0%), thyroid hormone ($n = 922$; 21.4%), antiepileptics ($n = 621$; 14.4%), anticoagulants ($n = 525$; 12.2%), bronchodilators and inhaled corticosteroids ($n = 382$; 8.9%), antidiabetics ($n = 262$; 6.1%)), antipsychotics ($n = 68$; 3.9%) and hormonal contraceptives ($n = 97$; 2.3%).

Comparison between women and men

Significant differences were found in some variables between women and men. It was found that cardiovascular, renal and urological comorbidities were more frequent in men, whereas rheumatologic comorbidities (immune and non-immune) were more frequent in women. Regarding pharmacological management, corticosteroids, chloroquine, azathioprine and mycophenolate were prescribed more to men, whereas hydroxychloroquine, methotrexate and leflunomide were prescribed more to women. Regarding comedications, analgesics were prescribed more to women, whereas antihypertensives, lipid-lowering drugs and anticoagulants were prescribed more to men (Table 1).

Comparison among geographical regions

The median age was higher in the Pacific Region than in the other regions. The proportion of patients with chronic comorbidities was lowest in the Caribbean Region, and cardiovascular diseases predominated in all regions. Patients in the Pacific Region had fewer prescriptions for corticosteroids and mycophenolate but more prescriptions for chloroquine, azathioprine and methotrexate than did the other regions. Deflazacort was widely used in the Central Region. The use of anticoagulants was predominant in the Bogotá-Cundinamarca Region (Table 2).

Comparison among age groups

Women represented the majority in all age groups. The proportion of comorbidities increased with increasing age. Cardiovascular diseases were predominant in all groups, but their frequency was higher in people older than 65 years. Prescriptions for corticosteroids decreased with increasing age, a trend that was observed with prednisolone and prednisone; for deflazacort, prescriptions increased with age. Chloroquine was predominant for those under 20 years of age, hydroxychloroquine was predominant for those between 20 and 39 years of age, and methotrexate was predominant for those over 40 years of age. Mycophenolate and cyclosporine were prescribed more frequently for children under 20 years of age. Anticoagulants and antiplatelet agents were prescribed more often for patients older than 65 years (Table 3).

Discussion

The prescription patterns of drugs used for patients diagnosed with SLE of any age and sex in a group of Colombian patients were identified, with characterizations of the differences or similarities in treatment according to age group, sex, and geographical region. SLE occurred more frequently in women, consistent with what is widely documented in other studies,[11–15] and the mean age (44.2 years) was in agreement with what was found in the United States (44.5–46.0 years)[12,16] Switzerland (44.8 years)[13] and Jamaica (45.1 years)[17] but higher than previously described in Canada (40.6 years)[18] and Colombia (38.4 years).[6]

Overall, corticosteroids were prescribed to 76.1% of patients, a similar rate to that found in the United States (78.8%)[16] but much more frequent than that reported for Canada (53.2%),[18] Puerto Rico (50.9%)[14] and Switzerland (48.0%).[13] Among DMARDs, the use of chloroquine stood out, differing markedly from reports in other studies where the use of hydroxychloroquine was predominant (43.4–91.3%).[11,13,16,17] The probable explanation for this result is that in Colombia, hydroxychloroquine is not included in the health benefits plan and has a higher cost compared to chloroquine, which can make access to it difficult.[19] However, chloroquine has been associated with greater adverse drug reactions and a worse safety profile, especially regarding the risk of retinopathy.[20] It was found that mycophenolate was prescribed more frequently in Colombia than in countries such as Korea (2.2%)[21] and the United States (3.3%),[11] whereas DMARDb were rarely used, similar to what has been reported in the literature.[11,21] In general, our hypothesis is that the differences and similarities found could be explained by the degree of activity and severity of SLE because in mild and moderate cases, antimalarials and corticosteroids are the recommended drugs, whereas when the disease progresses or is refractory, higher doses of corticosteroids, immunosuppressants or DMARDb are necessary[7–9]; however, we do not know the degree of disease activity in this cohort.

In addition to the above, cyclophosphamide that is indicated in patients with lupus nephritis[22] has been prescribed in 10.5% of patients in a Colombian cohort[6] and in 29.2% of patients in a Latin American cohort,[23] in marked contrast to the minimum proportion of patients who had it prescribed in this study. This is probably because cyclophosphamide when administered intravenously will require it to be performed in the hospital, and as the drug dispensing information used in this research only involves outpatient medications, it is highly likely that the patients who received this medication have not been fully identify them.

The prescription pattern for these drugs showed important differences when comparing women and men. There is limited information available in this regard; however, a study by Santamaría-Alza et al. that included 200 patients with SLE found significant differences in the use of cyclophosphamide between women and men (8.3% vs. 22.6%, respectively, $p = 0.017$),[6] a result that was not found in this study. In addition, they found no differences in the proportion of use of other

Table 1 – Comparison of sociodemographic, clinical and pharmacological variables according to sex for 4307 patients diagnosed with systemic lupus erythematosus in Colombia, 2019–2020.

Variables	Women		Men		*p*
	n = 3851	%	*n* = 456	%	
Age (median; IQR)	44.2 (32.6–55.7)		44.3 (31.2–57.2)		0.872
No chronic comorbidities	1095	28.4	136	29.8	0.534
With chronic comorbidities	2756	71.6	320	70.2	
Cardiovascular	1807	46.9	241	52.6	0.021
Rheumatological	1124	29.2	74	16.2	<0.001
Inmune	933	24.2	57	12.5	<0.001
Non-inmune	328	8.5	20	4.4	<0.001
Endocrine	893	23.2	89	19.4	0.070
Neurological	533	13.8	52	11.4	0.142
Psychiatric	359	9.3	31	6.8	0.072
Renal	269	7.0	49	10.7	0.004
Gastrointestinal	257	6.7	21	4.6	0.085
Respiratory	99	2.6	13	2.8	0.734
Cancer	91	2.4	9	2.0	0.593
Urinary	36	0.9	24	5.2	<0.001
Pharmacological management	–	–	–	–	–
DMARDs	3498	90.8	403	88.0	0.050
Chloroquine	2065	53.6	278	60.7	0.004
Azathioprine	1390	36.1	189	41.3	0.030
Hydroxychloroquine	1161	30.1	106	23.1	0.002
Methotrexate	694	18.0	64	14.0	0.031
Leflunomide	94	2.4	3	0.7	0.011*
Sulfasalazine	52	1.4	4	0.9	0.515*
Corticosteroids	2910	75.6	368	80.3	0.023
Prednisolone	2578	66.9	337	73.6	0.004
Prednisone	464	12.0	91	19.9	<0.001
Deflazacort	246	6.4	15	3.3	0.008
Methylprednisolone	144	3.7	12	2.6	0.225
Other immunosuppressants	716	18.6	121	26.4	<0.001
Mycophenolate	609	15.8	110	24.0	<0.001
Cyclosporine	104	2.7	10	2.2	0.514
Cyclophosphamide	30	0.8	6	1.3	0.269*
Tacrolimus	13	0.3	2	0.4	0.669*
DMARDb	11	0.3	0	0.0	0.620*
Belimumab	6	0.2	0	0.0	1.000*
Rituximab	3	0.1	0	0.0	1.000*
Adalimumab	2	0.1	0	0.0	1.000*
Comedications	3643	94.6	418	91.7	0.011
Non-opioid pain medications	2626	68.2	228	50.0	<0.001
Antiulcer	2172	56.4	219	48.0	0.001
Antihypertensives and diuretics	1961	50.9	273	59.9	<0.001
Platelet antiaggregants	1087	28.2	123	27.0	0.574
Lipid-lowering	917	23.8	161	35.3	<0.001
Antidepressants	934	24.3	83	18.2	0.004
Antihistamines	936	24.3	66	14.5	<0.001
Opioid pain medications	881	22.9	68	14.9	<0.001
Thyroid hormone	857	22.3	65	14.3	<0.001
Antiepileptic drugs	563	14.6	58	12.7	0.275
Anticoagulants	442	11.5	83	18.2	<0.001
Inhaled bronchodilators and corticosteroids	336	8.7	46	10.1	0.333
Antidiabetic	232	6.0	30	6.6	0.639
Antipsychotics	151	3.9	17	3.7	0.840

IQR: Interquartile range. DMARDs: synthetic disease-modifying antirheumatic drugs. DMARDb: biological disease-modifying antirheumatic drugs.

* Fisher's exact test.

Table 2 – Comparison of sociodemographic, clinical and pharmacological variables according to geographic region for 4307 patients diagnosed with systemic lupus erythematosus in Colombia, 2019–2020.

Variables	Bogota-Cundinamarca		Caribbean Region		Central Region		Pacific Region		Amazon-Orinoco and Eastern Region	
	n = 1491	%	*n* = 1036	%	*n* = 878	%	*n* = 753	%	*n* = 149	%
Woman	1288	86.4	940	90.7	806	91.8	684	90.8	133	89.3
Man	203	13.6	96	9.3	72	8.2	69	9.2	16	10.7
Age (median; IQR)	43.4 (31.2–56.2)		42.0 (32.4–51.4)		45.1 (33.1–56.5)		49.3 (35.3–60.3)		41.0 (30.5–54.8)	
No chronic comorbidities	332	22.3	427	41.2	197	22.4	243	32.3	32	21.5
With chronic comorbidities	1159	77.7	609	58.8	681	77.6	510	67.7	117	78.5
Cardiovascular	865	58.0	332	32.0	498	56.7	287	38.1	66	44.3
Rheumatological	376	25.2	236	22.8	299	34.1	253	33.6	34	22.8
Endocrine	419	28.1	160	15.4	208	23.7	132	17.5	63	42.3
Neurological	210	14.1	113	10.9	163	18.6	78	10.4	21	14.1
Psychiatric	118	7.9	51	4.9	138	15.7	59	7.8	24	16.1
Renal	131	8.8	59	5.7	61	6.9	55	7.3	12	8.1
Gastrointestinal	112	7.5	48	4.6	66	7.5	45	6.0	7	4.7
Respiratory	35	2.3	23	2.2	23	2.6	26	3.5	5	3.4
Cancer	34	2.3	19	1.8	26	3.0	14	1.9	7	4.7
Urinary	27	1.8	9	0.9	13	1.5	8	1.1	3	2.0
Pharmacological management	–	–	–	–	–	–	–	–	–	–
DMARDs	1369	91.8	915	88.3	795	90.5	684	90.8	138	92.6
Chloroquine	830	55.7	538	51.9	412	46.9	499	66.3	64	43.0
Azathioprine	570	38.2	373	36.0	299	34.1	295	39.2	42	28.2
Hydroxychloroquine	469	31.5	331	31.9	332	37.8	86	11.4	49	32.9
Methotrexate	287	19.2	119	11.5	168	19.1	159	21.1	25	16.8
Leflunomide	21	1.4	18	1.7	41	4.7	13	1.7	4	2.7
Sulfasalazine	16	1.1	8	0.8	18	2.1	14	1.9	0	0.0
Corticosteroids	1184	79.4	838	80.9	632	72.0	507	67.3	117	78.5
Prednisolone	1129	75.7	709	68.4	521	59.3	449	59.6	107	71.8
Prednisone	200	13.4	146	14.1	74	8.4	121	16.1	14	9.4
Deflazacort	46	3.1	57	5.5	120	13.7	27	3.6	11	7.4
Methylprednisolone	28	1.9	84	8.1	21	2.4	19	2.5	4	2.7

– Table 2 (*Continued*)

Variables	Bogota-Cundinamarca		Caribbean Region		Central Region		Pacific Region		Amazon-Orinoco and Eastern Region	
	n = 1491	%	*n* = 1036	%	*n* = 878	%	*n* = 753	%	*n* = 149	%
Other immunosuppressants	298	20.0	205	19.8	176	20.0	136	18.1	22	14.8
Mycophenolate	260	17.4	194	18.7	164	18.7	83	11.0	18	12.1
Cyclosporine	42	2.8	4	0.4	11	1.3	54	7.2	3	2.0
Cyclophosphamide	5	0.3	17	1.6	5	0.6	8	1.1	1	0.7
Tacrolimus	5	0.3	2	0.2	4	0.5	4	0.5	0	0.0
DMARDb	0	0.0	5	0.5	1	0.1	4	0.5	1	0.7
Belimumab	0	0.0	2	0.2	1	0.1	3	0.4	0	0.0
Rituximab	0	0.0	2	0.2	0	0.0	0	0.0	1	0.7
Adalimumab	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0
Comedications	1433	96.1	965	93.1	808	92.0	712	94.6	143	96.0
Non-opioid pain medications	1014	68.0	699	67.5	548	62.4	486	64.5	107	71.8
Antiulcer	721	48.4	657	63.4	486	55.4	441	58.6	86	57.7
Antihypertensives and diuretics	840	56.3	493	47.6	451	51.4	377	50.1	73	49.0
Platelet antiaggregants	463	31.1	249	24.0	237	27.0	227	30.1	34	22.8
Lipid-lowering	352	23.6	245	23.6	238	27.1	211	28.0	32	21.5
Antidepressants	306	20.5	205	19.8	266	30.3	185	24.6	55	36.9
Antihistamines	328	22.0	276	26.6	212	24.1	157	20.8	29	19.5
Opioid pain medications	312	20.9	225	21.7	262	29.8	107	14.2	43	28.9
Thyroid hormone	396	26.6	123	11.9	181	20.6	182	24.2	40	26.8
Anticonvulsants drugs	197	13.2	136	13.1	173	19.7	91	12.1	24	16.1
Anticoagulants	269	18.0	73	7.0	93	10.6	68	9.0	22	14.8
Inhaled bronchodilators and corticosteroids	145	9.7	114	11.0	56	6.4	57	7.6	10	6.7
Antidiabetic	82	5.5	67	6.5	58	6.6	47	6.2	8	5.4
Antipsychotics	34	2.3	30	2.9	55	6.3	38	5.0	11	7.4

IQR: Interquartile range. DMARDs: synthetic disease-modifying antirheumatic drugs. DMARDb: biological disease-modifying antirheumatic drugs.

Table 3 – Comparison of sociodemographic, clinical and pharmacological variables according to age group for 4307 patients diagnosed with systemic lupus erythematosus in Colombia, 2019–2020.

Variables	<20 years		20–39 years		40–64 years		≥65 years	
	n = 198	%	*n* = 1560	%	*n* = 2120	%	*n* = 429	%
Woman	168	84.8	1396	89.5	1906	89.9	381	88.8
Man	30	15.2	164	10.5	214	10.1	48	11.2
No chronic comorbidities	94	47.5	592	37.9	487	23.0	58	13.5
With chronic comorbidities	104	52.5	968	62.1	1633	77.0	371	86.5
Cardiovascular	68	34.3	621	39.8	1080	50.9	279	65.0
Rheumatological	18	9.1	298	19.1	694	32.7	188	43.8
Endocrine	25	12.6	238	15.3	580	27.4	139	32.4
Neurological	14	7.1	164	10.5	331	15.6	76	17.7
Psychiatric	5	2.5	100	6.4	237	11.2	48	11.2
Renal	9	4.5	114	7.3	148	7.0	47	11.0
Gastrointestinal	6	3.0	62	4.0	164	7.7	46	10.7
Respiratory	3	1.5	11	0.7	62	2.9	36	8.4
Cancer	3	1.5	26	1.7	57	2.7	14	3.3
Urinary	1	0.5	7	0.4	33	1.6	19	4.4
Pharmacological management	–	–	–	–	–	–	–	–
DMARDs	185	93.4	1437	92.1	1919	90.5	360	83.9
Chloroquine	149	75.3	877	56.2	1134	53.5	183	42.7
Azathioprine	78	39.4	612	39.2	747	35.2	142	33.1
Hydroxychloroquine	33	16.7	566	36.3	563	26.6	105	24.5
Methotrexate	23	11.6	250	16.0	400	18.9	85	19.8
Leflunomide	0	0.0	28	1.8	62	2.9	7	1.6
Sulfasalazine	0	0.0	14	0.9	34	1.6	8	1.9
Corticosteroids	172	86.9	1262	80.9	1549	73.1	295	68.8
Prednisolone	159	80.3	1140	73.1	1371	64.7	245	57.1
Prednisone	55	27.8	268	17.2	206	9.7	26	6.1
Deflazacort	4	2.0	86	5.5	130	6.1	41	9.6
Methylprednisolone	7	3.5	57	3.7	77	3.6	15	3.5
Other immunosuppressants	83	41.9	391	25.1	317	15.0	46	10.7
Mycophenolate	72	36.4	343	22.0	268	12.6	36	8.4
Cyclosporine	15	7.6	41	2.6	48	2.3	10	2.3
Cyclophosphamide	0	0.0	25	1.6	10	0.5	1	0.2
Tacrolimus	0	0.0	6	0.4	9	0.4	0	0.0
DMARDb	0	0.0	6	0.4	3	0.1	2	0.5
Belimumab	0	0.0	4	0.3	1	0.0	1	0.2
Rituximab	0	0.0	1	0.1	2	0.1	0	0.0
Adalimumab	0	0.0	1	0.1	0	0.0	1	0.2
Comedications	179	90.4	1454	93.2	2010	94.8	418	97.4
Non-opioid pain medications	84	42.4	991	63.5	1467	69.2	312	72.7
Antiulcer	98	49.5	762	48.8	1258	59.3	273	63.6
Antihypertensives and diuretics	107	54.0	725	46.5	1114	52.5	288	67.1
Platelet antiaggregants	45	22.7	416	26.7	594	28.0	155	36.1
Lipid-lowering	15	7.6	271	17.4	620	29.2	172	40.1
Antidepressants	14	7.1	282	18.1	597	28.2	124	28.9
Antihistamines	36	18.2	359	23.0	501	23.6	106	24.7
Opioid pain medications	12	6.1	306	19.6	528	24.9	103	24.0
Thyroid hormone	15	7.6	208	13.3	533	25.1	166	38.7
Anticonvulsants drugs	17	8.6	164	10.5	373	17.6	67	15.6
Anticoagulants	11	5.6	209	13.4	240	11.3	65	15.2
Inhaled bronchodilators and corticosteroids	9	4.5	104	6.7	187	8.8	82	19.1
Antidiabetic	2	1.0	37	2.4	171	8.1	52	12.1
Antipsychotics	2	1.0	49	3.1	96	4.5	21	4.9

DMARDs: synthetic disease-modifying antirheumatic drugs. DMARDb: biological disease-modifying antirheumatic drugs.

drugs used to manage SLE,[6] which contrasts with the results found in the present study, i.e., corticosteroid, chloroquine, azathioprine and mycophenolate prescriptions were predominant for men, whereas azathioprine and hydroxychloroquine prescription were predominant for women. These findings are related to the clinical differences and the frequency of complications between women and men; renal disease, serositis and thrombocytopenia are predominant in the latter.[24] In the United States, Pelletier et al. compared patients with and without lupus nephritis and found that the use of corticosteroids, immunosuppressants and antimalarials was more frequent in patients with kidney disease.[25]

Different clinical pictures of SLE have been observed in children and adults. In children, the disease is more active, with a much more aggressive progression and with more complications, which affects the type of treatment used.[3,15,26] In this analysis, prescription patterns were investigated according to age group, showing greater use of chloroquine, immunosuppressants and corticosteroids in patients under 20 years of age. A study conducted in Canada compared pediatric and adult patients with SLE and reported similar findings; i.e., corticosteroids (97.0% vs. 70.0%; $p < 0.0001$) and immunosuppressants (66.0% vs. 37.0%; $p = 0.0001$) were prescribed more to children, whereas methotrexate was prescribed more to adults (31.0% vs. 9.0%; $p = 0.009$).[15] In Hungary, it was found that mycophenolate was prescribed much more frequently to children than to adults (15.2% vs. 5.3%; $p = 0.0056$),[26] results that are similar to those for the United States (28.1 vs. 13.0; $p < 0.001$)[27] and in agreement with our results.

The drugs used for the management of SLE were prescribed differently among the different geographical regions of Colombia. This pattern had already been evidenced in another pharmacoepidemiological study that compared the prescription of ambulatory antibiotics in the different regions of the country[28] and is probably due to the prescribing habits of physicians, to the academic training of physicians, to the variability in the availability of drugs, to the influence of the pharmaceutical industry and to the health system affiliation regime. Thus, for example, in Argentina, cyclophosphamide was administered more frequently in the public health system than in the private system, while the use of corticosteroids, antimalarials and immunosuppressants was similar between the two systems.[29]

Finally, it is important to highlight that, during the study period, the first months of the mandatory preventive isolation (confinement) caused by the pandemic of Coronavirus Disease 2019 (COVID-19) in Colombia were included, without affecting the dispensing of drugs in patients with systemic lupus erythematosus present in the study.

Some limitations in the interpretation of the results are recognized because access to medical records was not obtained to verify the patients' diagnoses and their hospitalizations and the activity, severity and complications of the disease or comorbidity such as antiphospholipid antibody syndrome. In addition, the drugs prescribed outside the health system or that were not delivered by the dispensing company and the drug induction cycles that the patients may have received are unknown. However, the sample included many patients distributed throughout most of the Colombian territory and both the contributory and subsidized regimes.

Conclusions

Given the above findings, it can be concluded that there are differences in the prescription of drugs used for patients with SLE according to age group, sex and geographical regions of the country. Patients with SLE in Colombia are treated with DMARDs, especially chloroquine and azathioprine, with corticosteroids, particularly prednisolone, and with immunosuppressants such as mycophenolate, and infrequently receive DMARDb. In addition, they frequently have cardiovascular, rheumatologic and endocrine comorbidities and, in addition to drugs for the management of SLE, are prescribed nonopioid analgesics, antiulcers and antihypertensives. Knowledge of the differences in management found can be useful to guide treating physicians and health plan administrators to manage the resources necessary to meet the needs of this important group of patients.

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Conflict of interest

The authors declare no conflict of interest.

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