



# Epidemiology and management practices for childhood-onset systemic lupus erythematosus patients: a survey in Latin America

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## Abstract

To assess epidemiology and management practices of Latin America Pediatric Rheumatologists (LAPR) about childhood-onset systemic lupus erythematosus (cSLE). A cross-sectional study was performed in 288 LAPR PANLAR members based on online survey about cSLE practices. The response rate of web-based survey by LAPR was 170/288(59%) and the majority worked in university hospitals (63%). The ACR and/or SLICC classification criteria (99%) and disease activity tools (97%) were almost universally used by LAPR, whereas damage index (70%) and CHAQ (58%) instruments were less frequently used. Laboratory exams, diagnostic imaging, and biopsies were generally available (> 75%), however low availability for densitometry (66%). Drug access was excellent for the most common prescribed medications (> 75%), except for belimumab (11%). Emerging mosquito-borne diseases were also reported: dengue (20%), chikungunya (11%), and Zika (8%). Groups were further divided in two, according to the median number of cSLE patients followed by LAPR in the last year: groups A and B ( $\geq 25$  and  $< 25$ , respectively). Frequencies of condom in combination with other contraceptive methods were significantly higher in group A than B ( $p = 0.01$ ). The frequencies of reported pregnancy ( $p < 0.001$ ) and non-adherence to therapy were significantly higher in group A ( $p = 0.023$ ). Alcohol intake ( $p = 0.004$ ) and illicit drug use ( $p = 0.007$ ) were also reported more frequently by LAPR of group A in at least one cSLE patient. This first large web-based survey demonstrated an overall excellent access for diagnosis and therapy by LAPR, probably related to their high rate of practices in tertiary care of university hospitals. Adherence to therapy, pregnancy, and substance abuse was identified as major challenges in this population, particularly in larger centers.

**Keywords** Adolescent · Childhood-onset systemic lupus erythematosus · Children · Epidemiology · Latin America · Survey

## Introduction

Childhood-onset systemic lupus erythematosus (cSLE) is a rare chronic inflammatory autoimmune disease that may affect many organs and systems [1]. This disease has been reported around the world, with major impact due to ethnicity in Latin America (LA) populations [2–19].

LA includes 33 countries and dependencies, a large population, two main languages (Spanish and Portuguese), with distinct socio-economic and political status. Two groups have reported data focused on epidemiology, clinical and laboratorial features of cSLE patients in LA: BRAC-SLE (Brazilian Childhood-onset SLE Registry Group) [2–15] and GLADEL (Grupo Latino Americano De Estudio del Lupus) [16–19].

However, to the best of our knowledge, epidemiology and management of cSLE based on LA Pediatric Rheumatologists (LAPR) were not carried out.

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Therefore, the objective of the present cross-sectional survey study was to assess LAPR reports of cSLE patients regarding epidemiology, classification criteria, disease activity, and other instruments used in clinical practices, laboratory and other exams availability, general supportive care, drugs availability, infections, non-live vaccines, issues observed in adolescents, reproductive health issues, and transition-focused program to adult care. In addition, comparisons of epidemiology and management according to the number of cSLE patients followed during last year were also performed.

## Methods

A cross-sectional study was conducted in 288 LAPR, based on an online survey about cSLE practices. All physicians are members of Pan-American League of Association for Rheumatology (PANLAR).

This online survey was carried out using Research Electronic Data Capture (REDCap) tool. This is a secure web instrument proposed to support data capture for research studies, offering an interface for validated data entry. This tool also audits trails for tracking data manipulation, allows automated export procedures for statistical analyses, and permits importing data from external sources.

Between June and August 2017, a questionnaire was sent to all countries that had LAPR, which included 21 countries (Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Haiti, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Puerto Rico, Uruguay, and Venezuela). At least five emails were sent to improve the response rate. Ethics Committee of the coordinating center, a university hospital, approved this study.

The questionnaire was composed by 20 questions of physician-reported epidemiology and management practices for cSLE patients. These questions were of multiple choice-response or dichotomous (yes and no), recalling observations during the last year. Estimated time for responses was nearly 15 min.

The electronic survey included 20 questions related to the following topics:

1. Number and clinical features of cSLE patients followed in the last year by LAPR
2. Demographic data of LAPR [gender, years of LAPR practice, city, state, country, location of LAPR practice (public university practice, private university practice, public clinical practice, and/or private clinical practice)]
3. LAPR employment (part-time or full-time)
4. Health care insurance availability for cSLE patients (public health insurance, private insurance and/or other)
5. Classification criteria for cSLE diagnosis used by LAPR [none, 1997 American College of Rheumatology (ACR) criteria and/or 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria]
6. Disease activity tools used in clinical practices by LAPR [none, Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), Systemic lupus erythematosus disease activity index 2000 (SLEDAI-2K), Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA-SLEDAI), British Isles Lupus Assessment Group (BILAG), Physician global assessment, and/or Patient/parent global assessment]
7. Other tools used in clinical practices by LAPR [none, Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index, Simple Measure of the Impact of Lupus Erythematosus in Youngsters (SMILEY), Childhood Health Assessment Questionnaire (CHAQ), and/or Childhood Health Questionnaire (CHQ)]
8. Laboratory exams availability by LAPR [serum complement (C3, C4, and/or CH50), antinuclear antibodies (ANA), anti-dsDNA antibody, anti-Sm antibody, anti-RNP antibody, anti SSA/Ro antibody, anti SSB/La antibody, anti-ribosomal P (anti-P) antibody, lupus anticoagulant, anticardiolipin IgG, and/or anticardiolipin IgM]
9. Other exams availability by LAPR (bone densitometry, eye exam, lipid profile, 25 OH vitamin D, renal biopsy, cutaneous biopsy, electrocardiography, echocardiography, musculoskeletal ultrasound, and/or magnetic resonance imaging)
10. General supportive care recommended by LAPR [sunscreen protection (availability, routine advice availability and supportive staffs/team availability), physical activity orientation (availability, routine advice availability, and supportive staffs/team availability), multidisciplinary team approach, strict control of blood pressure (auscultatory blood pressure device availability, oscillometric blood pressure device availability, home measurement of blood pressure availability, ambulatory blood pressure monitor availability, anti-hypertensive drug availability, and nephrologist co-management), sexual function issues (questionnaires to assess sexual function availability, clinical history to assess sexual function availability, supportive staffs for counseling contraceptives availability), and/or transition plan to appropriate adult healthcare provider]
11. Inpatients and outpatients care facilities available for cSLE treatment (electronic medical chart, day hospital, dietary orientation, drugs prescription, phone calls for clinical assessments, appointments schedule, community resources support, palliative care support, psychological support, dental care, rehabilitation care, speech and language therapy, blood sample collection, joint

injection administration, intravenous therapy administration, counseling patients/family about the illness, clinical trials participation, patients/family education about the illness, drug compliance, appointments compliance, perform/teach physical activities, vital signs measurement, anthropometric data evaluation, vaccination card evaluation, health-related quality of life questionnaires, pain assessment evaluation, and/or adverse events monitoring)

12. Drugs availability for cSLE patients reported by LAPR (prednisone/prednisolone, intravenous methylprednisolone, chloroquine diphosphate, hydroxychloroquine sulfate, azathioprine, methotrexate, cyclosporine, mycophenolate mofetil, intravenous cyclophosphamide, rituximab, belimumab, and/or plasmapheresis)
13. Antimalarial prescription for cSLE patients (musculoskeletal manifestations, serositis, disease activity and always)
14. Infections diagnosed in cSLE patients—at least one infection (herpes zoster, dengue virus, Zika virus, chikungunya virus, yellow fever virus, bacterial sepsis, invasive fungal infections, tuberculosis, and/or Hansen disease)
15. Non-live vaccines prescribed for cSLE patients [annual influenza, pneumococcal, tetanus, hepatitis A, hepatitis B, meningococcal, human papillomavirus (HPV), and/or none of them]
16. Issues observed in adolescent cSLE patients—at least one issue (non-adherence of medications, smoking use, alcohol intake, illicit drug use, cancer, types of cancer, and/or pregnancy)
17. Contraception prescription for adolescent cSLE patients (condom, oral progesterone, depot medroxyprogesterone acetate, implant progesterone contraceptive, emergency contraception, intrauterine device, and/or none of them)
18. Strategies to prevent infertility for cSLE adolescents treated with intravenous cyclophosphamide (IVCYC) [gonadotropin-releasing hormone agonists (GnRHa), embryo or oocyte cryopreservation, sperm cryopreservation, cryobanking of ovarian tissue, cryobanking of testicular tissue, and/or none of them]
19. cSLE participation in any clinical trial (yes or no)
20. Transition-focused program to adult care (transfer based only on age, transition to an internal medicine physician, transition to rheumatologist clinic in the same rheumatology service, transition to rheumatologist clinic to another rheumatology service, and/or non-established program)

Groups were further subdivided in A and B according to the median number of cSLE patients followed by LAPR in the last year: group A ( $\geq 25$  patients in the last year) and group B ( $< 25$  patients).

## Statistical analysis

Data were presented in numbers (percentages) for categorical variables, and differences between groups A and B were assessed by Pearson chi-square or Fisher exact test, as appropriate. Data were presented in median (minimum to maximum value) or mean  $\pm$  standard deviation for continuous variables according to abnormal or normal distribution, respectively, and further comparisons between groups A and B were conducted using Mann-Whitney test or Student's *t* test, accordingly. *P* values less than 0.05 were considered significant.

## Results

The response rate for this web-based survey was 170/288 (59%) including 16/21 (76%) of the countries with at least one LAPR. The number of 170 surveyed specialists in each country was as follows: Brazil  $n = 85$  (50%), Argentina  $n = 22$  (13%), Mexico  $n = 22$  (13%), Colombia  $n = 11$  (6.5%), Chile  $n = 6$  (3.6%), Venezuela  $n = 3$  (1.8%), Paraguay  $n = 2$  (1.1%), Ecuador  $n = 2$  (1.1%), Nicaragua  $n = 2$  (1.1%), Peru  $n = 2$  (1.1%), Bolivia  $n = 1$  (0.6%), Costa Rica  $n = 1$  (0.6%), Dominican Republic  $n = 1$  (0.6%), El Salvador  $n = 1$  (0.6%), Panama  $n = 1$  (0.6%), Uruguay  $n = 1$  (0.6%), and absence of country reported  $n = 7$  (4.1%). Incomplete data was observed in  $n = 9/170$  (5.3%), and therefore 161/170 responses were evaluated.

The main clinical features of cSLE patients reported by 161 LAPR were: nephritis in 138 (86%), skin manifestations in 136 (84%), hematological involvement in 135 (84%), musculoskeletal manifestations in 116 (72%), fever in 114 (71%), serositis in 79 (49%), neuropsychiatric manifestations in 52 (32%), Raynaud phenomenon in 38 (24%), pulmonary manifestations in 22 (14%), gastrointestinal involvement in 20 (12%) and ocular involvement in 8 (5%)

Table 1 shows demographic data, countries, classification criteria, disease activity and other tools used, laboratory, and other exam availability in cSLE patients followed during last year and reported by LAPR. The ACR or SLICC classification criteria (99%) and disease activity tools (97%) were almost universally used by LAPR, whereas damage index (70%) and CHAQ (58%) instruments were less frequently used. Laboratory exams, diagnostic imaging, and biopsies were generally available ( $> 75\%$ ), however a low availability for densitometry (66%) and anti-ribosomal P antibody (47%). The majority of LAPR had also access to other diagnostic interventions, such as renal (83%) and cutaneous biopsies (87%). With regard to general supportive care, only 66% reported sexual function orientation and the majority ( $> 75\%$ ) had availability for blood pressure control, physical activity recommendation, sunscreen protection, and multidisciplinary team approach. In spite of that, other supportive care access

**Table 1** Demographic data, countries, classification criteria, disease activity and other tools used, and laboratory, diagnostic imaging, eye exam, and biopsies availability in cSLE patients followed during last year and reported by Latin America Pediatric Rheumatologists (LAPR)

Variables	LAPR response (n = 161)
<b>Demographic data</b>	
Female gender	118 (73)
<b>Countries</b>	
Brazil	85 (53)
Argentina	22 (14)
Mexico	22 (14)
Others	32 (20)
<b>Local of practice</b>	
Public/private university	103 (64)
Only public clinical practice	38 (24)
Only private clinical practice	20 (12)
<b>Health care insurance</b>	
Public/private health insurance	74 (46)
Only public health insurance	55 (34)
Only private health insurance	32 (20)
<b>LAPR employment</b>	
Full-time work	62 (38)
<b>Classification criteria used</b>	
ACR and/or SLICC criteria	159 (99)
<b>Disease activity tools used</b>	
SLEDAI/SLEDAI-2K/SELENA-SLEDAI or BILAG	157 (97)
<b>Other tools used</b>	
SLICC/ACR-DI	113 (70)
SMILEY	12 (7)
CHAQ	93 (58)
CHQ	13 (8)
<b>Laboratory exams availability</b>	
Serum complement	158 (98)
ANA	157 (97)
Anti-dsDNA antibody	154 (96)
Anti-Sm antibody	146 (91)
Anti-RNP antibody	142 (88)
Anti SSA/Ro antibody	146 (91)
Anti SSB/La antibody	146 (91)
Anti-ribosomal P antibody	76 (47)
Lupus anticoagulant	144 (89)
Anticardiolipin IgM antibody	151 (94)
Anticardiolipin IgG antibody	151 (94)
Lipid profile	158 (98)
25,OH vitamin D	133 (83)
<b>Diagnostic imaging, eye exam, and biopsy availability</b>	
Bone densitometry (DEXA scan)	106 (66)
Eye exam	152 (94)
Renal biopsy	134 (83)
Cutaneous biopsy	141 (87)
Electrocardiography	155 (96)

**Table 1** (continued)

Variables	LAPR response (n = 161)
Echocardiography	157 (97)
Musculoskeletal ultrasound	133 (83)
Magnetic resonance imaging	125 (78)

Results are presented in *n* (%)

*cSLE* childhood-onset systemic lupus erythematosus, *ACR* American College of Rheumatology, *ANA* antinuclear antibodies, *SLEDAI-2K* Systemic Lupus Erythematosus Disease Activity Index 2000, *SLICC/ACR-DI* Systemic Lupus International Collaborating Clinics/ACR-Damage Index, *BILAG* British Isles Lupus Assessment Group, *SMILEY* Simple Measure of the Impact of Lupus Erythematosus in Youngsters, *CHAQ* Childhood Health Assessment Questionnaire, *CHQ* Childhood Health Questionnaire, *DEXA* dual-energy X-ray absorptiometry

such as phone call for clinical assessment, community resources support, palliative care support, psychological support, drug compliance, dental care, rehabilitation care, family/patients counseling, adverse events monitoring, and speech language therapy consultation were reported to be available by less than 70% of the LAPR (Table 2).

Drug access was excellent for the most commonly prescribed medications in pediatric rheumatology (> 75%), except for belimumab (11%). The majority of LAPR (92%) reported antimalarial prescription for all cSLE patients (Table 3).

Endemic illnesses were reported by LAPR in at least one cSLE patient during the previous year: tuberculosis (16%) and Hansen disease (2%). Emerging mosquito-borne diseases were also reported in at least one patient in the same period by LAPR in Central America and in the Brazil, Colombia, Peru, and Venezuela: dengue (20%), chikungunya (11%), and Zika (8%). There were no reports of yellow fever.

The contraceptive method most often prescribed by LAPR was condom (83%), with a much lower frequency for condoms combined with other contraceptive methods (59%). A limited access to transition-focused program to adult care (61%) was observed. Ninety percent of LAPR had no strategies to prevent IVCYC infertility. Non-adherence to medication (97%) was observed in at least one adolescent cSLE patient in the previous year, and it was the main issue reported by LAPR. Cancer was reported by 10/161 (6%) LAPR. The types of cancer developed during cSLE course were non-Hodgkin lymphoma in 9/161 (5%) and ovarian cystic teratoma in 1/161 (1%) (Table 3).

Groups were further divided into two according to the number of cSLE patients followed by LAPR in the last year: group A ( $\geq 25$  patients in the last year) and group B (< 25 patients). A higher frequency of full-time job (55 vs. 21%,  $p < 0.0001$ ) and work in a public university hospital (65 vs. 40%,  $p = 0.001$ ) was observed in group A compared to group

**Table 2** Availability of general and other supportive care in cSLE patients followed reported during last year by Latin America Pediatric Rheumatologists (LAPR)

Variables	LAPR response (n = 161)
General supportive care availability	
Sunscreen protection availability	158 (98)
Routine advice	133 (83)
Supportive staffs/team availability	32 (20)
Physical activity orientation availability	124 (77)
Routine advice	116 (72)
Supportive staffs/team availability	19 (12)
Multidisciplinary team approach	127 (79)
Control of blood pressure	94 (58)
Auscultatory blood pressure device availability	60 (37)
Oscillometric blood pressure device availability	14 (9)
Home measurement of blood pressure availability	44 (27)
Ambulatory blood pressure monitor availability	31 (19)
Anti-hypertensive drug availability	66 (41)
Nephrologist co-management	65 (40)
Sexual function orientation	60 (37)
Questionnaire to assess sexual function availability	11 (7)
Clinical history to assess sexual function availability	41 (25)
Supportive staffs for counseling	34 (21)
Contraceptives availability	43 (27)
Other supportive care availability	
Electronic medical chart	60 (37)
Day hospital	112 (69)
Dietary recommendation	124 (77)
Drugs prescription	135 (84)
Clinical assessments by phone calls	27 (17)
Appointments schedule	90 (56)
Community resources support	20 (12)
Palliative care support	51 (32)
Psychological support	78 (48)
Dental care	90 (56)
Rehabilitation care	99 (61)
Speech therapy orientation	33 (20)
Blood sample collection	135 (84)
Joint injection administration	126 (78)
Intravenous therapy administration	150 (93)
Counseling patients/family about the illness	103 (64)
Clinical or trials participation	74 (46)
Patients/family education about the illness	89 (55)
Drug compliance	68 (42)
Appointments compliance	44 (27)
Vital signs measurement	103 (64)
Anthropometric data evaluation	133 (83)
Vaccination card evaluation	133 (83)
Health-related quality of life questionnaires	70 (43)
Pain assessment evaluation	91 (56)
Adverse events monitoring	111 (69)

Results are presented in n (%)

cSLE childhood-onset systemic lupus erythematosus

**Table 3** Treatment availability, antimalarials prescription, infections diagnosed, non-live vaccines and contraceptive prescriptions, strategies to prevent IVCYC infertility, clinical trial participation, transition-focused program to adult care, and issues observed in cSLE adolescents followed during last year and reported by Latin America Pediatric Rheumatologists (LAPR)

Variables	LAPR response (n = 161)
Treatment availability	
Prednisone/prednisolone	153 (95)
Intravenous methylprednisolone	157 (97)
Antimalarials	151 (94)
Azathioprine	147 (91)
Methotrexate	150 (93)
Cyclosporine	128 (79)
Mycophenolate mofetil	132 (82)
Intravenous cyclophosphamide	156 (97)
Rituximab	122 (76)
Belimumab	18 (11)
Plasmapheresis	83 (51)
Antimalarial prescription	
Used for all cSLE patients	148 (92)
Infections diagnosed (at least one cSLE patient)	
Herpes zoster	126 (78)
Dengue virus	32 (20)
Zika virus	13 (8)
Chikungunya virus	18 (11)
Yellow fever virus	0 (0)
Bacterial sepsis	82 (51)
Invasive fungal infections	23 (14)
Tuberculosis	26 (16)
Hansen disease	4 (2)
Non-live vaccines prescription	
Annual influenza	149 (92)
Contraceptive prescription	
Condom	134 (83)
Condom in combination with other method	95 (59)
Oral progesterone	80 (50)
Depot medroxyprogesterone acetate	56 (35)
Implant progesterone contraceptive	15 (9)
Emergency contraception	17 (11)
Intrauterine device	21 (13)
Transition-focused program to adult care	99 (61)
Strategies to prevent IVCYC infertility	
GnRH $\alpha$	12 (7)
Embryo or oocyte cryopreservation	5 (3)
Sperm cryopreservation	4 (2)
None of them	145 (90)
Clinical trial participation	
cSLE patients participated in clinical trial	40 (25)
Issues observed in cSLE adolescents (at least one patient)	
Non-adherence of medications	156 (97)

**Table 3** (continued)

Variables	LAPR response (n = 161)
Smoking	34 (21)
Alcohol intake	51 (32)
Illicit drug use	20 (12)
Cancer	10 (6)
Non-Hodgkin lymphoma	9 (5)
Ovarian cystic teratoma	1 (1)
Pregnancy	54 (33)

Results are presented in n (%)

cSLE childhood-onset systemic lupus erythematosus, IVCYC Intravenous cyclophosphamide, GNRHa gonadotropin-releasing hormone agonist

B. A significantly lower frequency of only private health insurance was observed in group A compared to group B (12 vs. 28%,  $p = 0.0100$ ). LAPR of group A reported more often at least one cSLE patient during the previous year with herpes zoster (88 vs. 67%,  $p = 0.001$ ), bacterial sepsis (64 vs. 36%,  $p < 0.001$ ), and invasive fungal infections (21 vs. 6%,  $p = 0.006$ ) than group B (Table 4).

Regarding contraception, the frequencies of condom in combination with other contraceptive methods were significantly higher in group A than group B (69 vs. 48%,  $p = 0.01$ ), such as oral progesterone (59 vs. 39%,  $p = 0.007$ ), depot medroxyprogesterone acetate (45 vs. 23%,  $p = 0.003$ ), emergency contraception (17 vs. 4%,  $p = 0.007$ ), and intrauterine device use (20 vs. 5%,  $p = 0.004$ ). In spite of that, the frequency of reported pregnancy by LAPR was higher in group A (50 vs. 16%,  $p < 0.001$ ). Alcohol intake (42 vs. 21%,  $p = 0.004$ ) and illicit drug use (19 vs. 5%,  $p = 0.007$ ) were reported more frequently by LAPR of group A in at least one cSLE patient in the previous year compared to group B (Table 4).

The frequency of non-adherence to the therapy was similar in LAPR that reported only public health insurance compared to those that reported only private health insurance [52/55 (95%) vs. 30/32 (94%),  $p = 1.000$ ].

## Discussion

This is the first large web-based survey of epidemiology and management of cSLE based on LAPR practices. The great advantage of the present study was the large LAPR population of PANLAR members and the representation of the majority of LA countries. The majority had their practice in university hospitals. The high response rate, in spite of the lack of pay incentive, contrasts with the previous reports of surveys in pediatric chronic rhinosinusitis according to American Rhinologic Society (7%) [20], in cSLE nephritis based on PR and pediatric nephrologists data (15%) [21] and perception

of SLE quality indicators in North America (19%) [22]. The limitation of the present study was the convenience sample of PANLAR members and the possibility of memory bias of the respondents, since the questions were based on observation of cSLE practices during the last year.

Availability of diagnostic tests and therapy was beyond the expectation. The overall evaluation revealed that almost all parameters included in the quality of medical care in cSLE patients were available for LAPR [23]. We believe that the availability reported may not indicate easy access since in our experience in Brazil, the prescription of high cost drugs is usually followed by a long and time-consuming bureaucratic process with several restrictions that may limit its use.

We confirmed and extended previous observation that renal biopsy access is lower in Latin America than USA and further demonstrated that for LA, the rate is higher than previously reported in two centers in Brazil [23]. This procedure was provided more often by large centers. Bone densitometry access was lower than others diagnostic imaging, but within the range reported in three other USA centers [23]. With regard to supportive care related to the multidisciplinary team care, the availability was high for general supportive care. Conversely, we identified limited access for specialized multidisciplinary approach required for satisfactory care, such as psychological support, dental care, palliative care support, and speech and language therapy. Indeed, the relevance of the availability of these resources for better management of cSLE was previously emphasized [24, 25].

The most relevant issue observed by LAPR was the non-adherence of medication, in spite of high frequencies of glucocorticosteroid, antimalarials, and immunosuppressive availability. Compliance is a determinant factor on cSLE outcome [26–28], and Brazilian Society of Rheumatology Consensus for SLE reinforced the importance to evaluate adherence in all appointments, especially for adolescents [29]. Furthermore, alcohol intake and illicit drug were also important issues evidenced in adolescents, particularly reported by LAPR in large centers. These results may be due to the easier access of these substances in LA [30], despite the public health policies in many of the countries.

The majority of the cSLE patients followed by LAPR in large centers seemed to be from a low socioeconomic and low educated cohort of lupus, since over three-quarters of the patients were from the public university setting. In addition, approximately 10% of LAPR had access only to private health insurance.

Severe infections were a relevant issue, such as herpes zoster, bacterial sepsis, and invasive fungal infections, and they were more often observed in large centers. In fact, infections are an important cause of morbidity and mortality in cSLE populations associated with systemic, active disease and under immunosuppressive therapy [2–4, 31, 32]. Of note, in LA, emerging infectious diseases (chikungunya, dengue,

**Table 4** Demographic data, countries, biopsies, infections diagnosed, non-live vaccines and contraceptive prescription, and issues observed in cSLE adolescents according to the number of cSLE patients followed during last year and reported by Latin America Pediatric Rheumatologists (LAPR): group A ( $\geq 25$  patients/year) and group B ( $< 25$  patients/year)

Variables of LAPR	Group A (n = 84)	Group B (n = 77)	P
<b>Demographic data</b>			
Female gender	59 (70)	59 (77)	0.231
Number of cSLE patients	50 (25–300)	10 (0–24)	<i>&lt; 0.001</i>
LAPR practice duration, years	13.5 (1–45)	10 (1–34)	0.052
<b>Countries</b>			
Brazil	49 (58)	36 (42)	0.157
Argentina	8 (36)	14 (64)	0.167
Mexico	12 (55)	10 (45)	0.823
Others	15 (18)	17 (22)	0.556
<b>Local of LAPR practice</b>			
Public/private university	64 (76)	39 (51)	<i>0.001</i>
<b>LAPR employment</b>			
Full-time work	46 (55)	16 (21)	<i>&lt; 0.0001</i>
<b>Health care insurance</b>			
Public/private health insurance	48 (57)	26 (34)	<i>0.0043</i>
Only public health insurance	26 (31)	29 (38)	0.4080
Only private health insurance	10 (12)	22 (28)	<i>0.0100</i>
<b>Biopsy availability</b>			
Renal	77 (92)	57 (74)	<i>0.002</i>
Cutaneous	74 (88)	67 (87)	0.511
<b>Infections diagnosed (at least one cSLE patient)</b>			
Herpes zoster	74 (88)	52 (67)	<i>0.001</i>
Dengue virus	18 (21)	14 (18)	0.376
Zika virus	7 (8)	6 (8)	0.566
Chikungunya virus	10 (12)	8 (10)	0.480
Yellow fever virus	0 (0)	0 (0)	1.000
Bacterial sepsis	54 (64)	28 (36)	<i>&lt; 0.001</i>
Invasive fungal infections	18 (21)	5 (6)	<i>0.006</i>
Tuberculosis	17 (20)	9 (12)	0.104
Hansen disease	2 (2)	2 (3)	0.656
<b>Contraceptive prescription</b>			
Condom	74 (88)	60 (78)	0.065
Condom in combination with other method	58 (69)	37 (48)	<i>0.010</i>
Oral progesterone	50 (59)	30 (39)	<i>0.007</i>
Depot medroxyprogesterone acetate	38 (45)	18 (23)	<i>0.003</i>
Implant progesterone contraceptive	9 (11)	6 (8)	0.359
Emergency contraception	14 (17)	3 (4)	<i>0.007</i>
Intrauterine device	17 (20)	4 (5)	<i>0.004</i>
<b>Issues observed in cSLE adolescents (at least one patient)</b>			
Non-adherence of medications	84 (100)	72 (93)	<i>0.023</i>
Smoking	20 (24)	14 (18)	0.249
Alcohol intake	35 (42)	16 (21)	<i>0.004</i>
Illicit drug use	16 (19)	4 (5)	<i>0.007</i>
Cancer	7 (8)	3 (4)	0.202
Pregnancy	42 (50)	12 (16)	<i>&lt; 0.001</i>

Results are presented in n (%) and median (range). The italics forms only indicated p value < 0.05

cSLE childhood-onset systemic lupus erythematosus, ACR American College of Rheumatology, ANA antinuclear antibodies, SLEDAI-2K Systemic Lupus Erythematosus Disease Activity Index 2000, SLICC/ACR-DI Systemic Lupus International Collaborating Clinics/ACR-Damage Index, BILAG British Isles Lupus Assessment Group, SMILEY Simple Measure of the Impact of Lupus Erythematosus in Youngsters, CHAQ Childhood Health Assessment Questionnaire, CHQ Childhood Health Questionnaire

and Zika) are relevant differential diagnosis for mosquito-borne viral infections, particularly in endemic areas [33], as demonstrated herein by the report of at least 20% of the LAPR.

Regarding reproductive health, condom was the most often prescribed contraceptive method despite the high rate of non-adherence reported by LAPR. The recommendation of supervised injection or implant progesterone contraceptive in day hospital [34, 35] combined with condom should be reinforced to avoid the high rate of pregnancies reported by LAPR.

Female and male strategies to prevent infertility in cSLE patients under IVCYC use were rarely reported by LAPR, probably due to the high financial cost of these medications [36–38]. Well-established transition programs are still a challenge in LA clinical practice. A recent survey to assess transition practices in Brazil showed that only 14% of the pediatric rheumatologists were satisfied with their current transition process [39].

The most important clinical features reported by LAPR were nephritis, skin, hematological, musculoskeletal, fever, serositis, and neuropsychiatric. Renal involvement, hematological, seizure, and ocular manifestations, vasculitis, and fever were significantly higher in cSLE compared to adult SLE patients [40].

In conclusion, this survey demonstrated overall excellent access to diagnosis and therapy for cSLE, probably related to their high rate of specialists practice in university hospitals. Adherence to therapy, pregnancy, and substance abuse was identified as major challenges in this population particularly in larger centers.

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## Compliance with ethical standards

**Disclosures** None.

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