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Influenza and pneumococcal vaccination coverage in Latin American patients with systemic lupus erythematosus: a cross-sectional and comparative study

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Abstract

Background: Infections are a major cause of morbidity and mortality in systemic lupus (SLE). Vaccination would be an effective method to reduce infection rate. Coverage for influenza and pneumococcus appears to be low in Latin America. The objective of this study was to evaluate vaccination coverage for influenza and pneumococcus in Latin America, causes of non-vaccination and to compare it with European patients.

Methods: A survey was conducted through social networks targeting Latin American lupus patients. A self-report was used to assess the demographics, risk factors for pneumonia, vaccination status, and causes of non-vaccination. The same method was used for European patients. We used binary logistic regression to identify factors associated with pneumococcal and influenza vaccination.

Results: There were 1130 participants from Latin America. Among them, 97% were women with an average of 37.9 years (SD: 11.3) and 46.5% had more than 7 years of disease duration. Two or more risk factors for pneumonia were found in 64.9%. Coverage for influenza and pneumococcal was 42.7 and 25% respectively, being lower than in Europe. Tetanus coverage was the most important predictor for receiving influenza and pneumococcal vaccination. Lack of prescription was the most common cause of non-application (64.6%).

Conclusions: Vaccination coverage for influenza and pneumonia is low in Latin America, especially compared to Europe. It is necessary to make specialists aware of their role in vaccine control and to implement measures to improve coordination between them and general practitioners.

Keywords: Systemic lupus erythematosus, Vaccination coverage, Influenza vaccine, Pneumococcal vaccine, Latin America

Introduction

Infections are a major cause of morbidity and mortality in systemic lupus erythematosus (SLE) [1]. Nearly half of deaths from infections are attributed to pneumonia [2]. Patients with SLE are at increased risk of infection due to several factors such as the underlying condition [3], disease activity [4, 5] and the use of immunosuppressive

agents [6], although some treatments such as hydroxychloroquine may decrease this risk [7]. Vaccination would be an effective method to decrease morbidity and mortality from infections in SLE.

The European League Against Rheumatism (EULAR) recommends that vaccination against influenza (flu) and pneumococcus should be strongly considered for most adult patients with SLE, in particular those treated with immunosuppressive therapy or who have other medical conditions of high-risk for pneumonia (e.g., chronic bronchitis) [8]. Both vaccines have acceptable

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immunogenicity and are safe in these patients [9–11]. These vaccines should preferably be administered during inactive disease but may also be considered for use in patients with active disease [8].

SLE coverage for influenza and pneumococcus does not exceed 60% in many countries [12, 13]. The main reasons for non-vaccination are lack of recommendation from their treating physician or rejection by patients [13–16]. The use of prednisone at doses ≥ 7.5 mg and high age are predictors of receiving these vaccines [16].

There are few works on this subject in Latin America. A recent study conducted in Brazil [13] showed that the percentage of influenza vaccination in patients with SLE is less than 50%. In order to implement policies on vaccination in this population, it is necessary to know the scope of this problem at the regional level. For this reason, the authors decided to carry out this study.

The main objective of this study was to assess the degree of influenza and pneumococcal vaccination coverage in SLE patients in Latin America and to identify causes and predictors of non-vaccination. The secondary objective was to compare these data with those of European patients.

Methods

The survey was conducted using a self-administered questionnaire and disseminated through social networks, mainly Facebook. To avoid diagnostic bias, it was disseminated only through SLE associations and patient groups on Facebook. The questionnaire included questions to assess the demographics, risk factors for pneumonia, vaccination status, and causes for non-vaccination. For the composition of the questionnaire, validated questionnaires in Spanish [17, 18], English [19–22], Portuguese [23–25], French [26, 27] and Italian [28] were used as a basis. Once the final questionnaire was composed, it was translated into these five languages. Before publishing the survey, the questionnaires were shown to the patient associations to check their comprehension and to evaluate possible linguistic differences (e.g. between Latin Spanish and Spanish).

Data collection began in October 2018 and ended in November 2019. For the sample calculation, the number of patients with SLE in Latin America was estimated at 422400. This value arises from an average prevalence of SLE of 66 per 10,000 inhabitants [29] for a population of approximately 640 million [30]. The Pan American Health Organization (PAHO) in 2017 reported that the level of influenza vaccination coverage ranged from 32% (Uruguay) to 100% (Panama) and in older adults and from 55% (Argentina) to 100% (Mexico) in patients with chronic diseases [31]. Thus, a 50% coverage level was chosen for the sample calculation, with a 3% error. The

calculated sample, using the finite population correction, was 1064.

Case ascertainment and variables included in database

Participants over 18 years of age with a diagnosis of SLE who consented to participate and had completed the questionnaire in full were included. The survey was completely anonymous. To avoid duplicates, participants were asked to enter an email address without the domain. No duplicates were found.

Demographic data were collected on gender, date of birth, and country of residence. The general risk factors for pneumonia evaluated were: diabetes, smoking, and chronic cardiac, respiratory and renal pathologies. Diagnosis of diabetes was evaluated with a simple question: "Have you ever been told by a doctor that you have diabetes or do you take medication for diabetes? To assess smoking status (including cigarettes, cigars and pipes), they were asked whether they smoked currently, had quit less than or more than 6 months ago, or had never smoked. For the purposes of the study, smokers were defined as those who currently smoked or had quit less than six months ago. Chronic heart disease was evaluated with a simple question: "Have you ever been told by a doctor that you have a heart disease like valve disease, ischemic heart disease or heart failure, or do you take medication for the heart?" Similarly, chronic respiratory and renal diseases were evaluated with these questions: "Has a doctor ever told you that you have a respiratory illness such as asthma, chronic bronchitis, or COPD, or do you use inhalers?" and "Has a doctor ever told you that you have a renal disease such as kidney failure, or do you need to do dialysis?" All the questions mentioned above were closed-ended. For the purposes of this work, age over 50 years was considered a risk factor for pneumonia [32].

Vaccination status was assessed using two questions adapted from a validated self-report [19]: "Did you receive the flu vaccine this year" and "Did you receive at least one dose of pneumonia vaccine" Given that tetanus vaccination is widely distributed throughout the world in all age groups, we asked about its coverage to assess the overall vaccination rate in the region. To assess causes of non-vaccination, participants were asked to choose one or more of the following options: "Not indicated by doctor", "not available", "related to costs / problems with health insurance coverage", "vaccination refusal" and "others".

SLE-specific data were collected on duration of illness, current use of immunosuppressors and hydroxychloroquine, use of corticosteroids, and average monthly dose. For the purposes of this work, SLE activity was defined as self-reference of flare-ups occurred < 6 months ago [33] diagnosed by a doctor.

Statistical analysis

Continuous variables were summarized using mean, standard deviation (SD) and range, and analyzed with the Student-t-test. Categorical variables were expressed as numbers, percentages and analyzed with the chi-squared test.

We used binary logistic regression to identify factors associated with pneumococcal and influenza vaccination. Variables that were significant in the univariate analysis ($p < 0.10$) were included in the adjusted model. Odds ratio (OR) and adjusted OR with 95% confidence intervals (95% CI) was reported. Statistical significance was set at p value < 0.05 (2-tailed). Factors proposed for the analysis were: age > 50 years, diabetes, smoking, chronic cardiac/respiratory/renal disease, SLE activity, disease duration > 7 years, current use of immunosuppressors and use of ≥ 7.5 mg prednisone or equivalent, and a history of tetanus vaccination.

Analyses were conducted using Stata version 12.0 and Epidat version 3.1.

Results

Latin America

In total there were 1196 participants from Latin America. Sixty six were excluded because they did not meet inclusion criteria. Seven countries contributed more than 50

patients each, constituting 87.2% of the sample: Argentina, Mexico, Brazil, Chile, Peru, Colombia and Uruguay. Demographic data, risk factors for pneumonia, and SLE-specific information are shown in Table 1. Most of the patients were women under 40 years, with more than 5 years of disease duration. More than 60% had two or more risk factors for pneumonia, the most frequent being the use of immunosuppressors and corticosteroids, and SLE activity. Hydroxychloroquine use exceeded 50% in the entire region, reaching almost 90% in some countries.

Data on vaccination coverage are shown in Table 2. Overall, coverage for influenza and pneumonia did not exceed 50 and 25% respectively. These vaccination rates were consistent with coverage for tetanus, which did not exceed 50%. However, the vaccination coverage rate was found to be highly heterogeneous among the countries of the region. While in Argentina coverage for influenza and pneumococcus reached 65 and 55% respectively, in Mexico it was less than 20%. The most frequent ($> 60\%$) reported cause of non-vaccination in all countries was lack of prescription or medical recommendation. Issues related to availability or cost of vaccines were less than 13% of the causes of non-vaccination.

Considering that vaccination is recommended in patients receiving immunosuppressants and/or prednisone

Table 1 Demographics, risk factors for pneumonia, and SLE-specific data of Latin American patients*

	Argentina (265)	Mexico (214)	Brazil (190)	Chile (99)	Peru (96)	Colombia (63)	Uruguay (59)	All patients (1130)**
Age, years (SD)	39.7 (10.9)	36.2 (11.1)	36.7 (10.4)	37.4 (11.3)	37.7 (10.6)	37.8 (13.7)	44 (12.5)	37.9 (11.3)
Female	260 (98.1)	209 (97.7)	186 (97.9)	95 (96)	91 (94.8)	60 (95.2)	59 (100)	1096 (97)
Patients > 50 years	51 (19.2)	24 (11.2)	25 (13.2)	15 (15.2)	12 (12.5)	12 (19)	18 (30.5)	171 (15.1)
Disease duration, years (range)	7 (0–40)	6 (0–39)	6 (0–32)	5 (0–32)	5 (0–34)	5 (1–28)	8 (1–30)	6 (0–40)
Disease duration > 7 years	126 (47.5)	106 (49.5)	92 (48.4)	86 (86.9)	44 (45.8)	31 (49.2)	29 (49.1)	525 (46.5)
Immunosuppressors ^a	226 (85.3)	193 (90.2)	151 (79.5)	81 (81.8)	86 (89.6)	56 (63)	49 (83.1)	972 (86)
SLE activity ^b	153 (58)	111 (51.9)	142 (74.7)	56 (56.6)	48 (50)	42 (66.7)	39 (66.1)	674 (59.6)
Corticosteroid use ^c	91 (34.9)	67 (32.4)	105 (55.9)	44 (46.3)	36 (50)	29 (48.3)	22 (39.3)	445 (40.5)
Hydroxychloroquine	236 (89.1)	114 (53.3)	138 (72.6)	86 (86.9)	76 (79.2)	48 (76.2)	49 (83.1)	858 (75.9)
Smoking ^d	64 (24.2)	31 (14.5)	25 (13.2)	29 (29.3)	9 (9.4)	15 (23.8)	25 (42.4)	209 (18.5)
Chronic renal disease	52 (19.6)	34 (15.9)	39 (20.5)	17 (17.2)	19 (19.8)	17 (27)	8 (13.6)	202 (17.9)
Chronic respiratory disease	25 (9.4)	26 (12.1)	18 (9.5)	15 (15.2)	19 (19.8)	8 (12.7)	13 (22)	149 (13.2)
Chronic cardiac disease	24 (9.1)	14 (6.5)	20 (10.5)	8 (9.1)	12 (12.5)	9 (14.3)	12 (20.3)	110 (9.7)
Diabetes	11 (4.2)	13 (6.1)	11 (5.8)	10 (10.1)	6 (6.3)	8 (12.7)	6 (10.2)	72 (6.4)
> 1 risk factors for pneumonia ^e	176 (66.4)	129 (60.3)	150 (78.9)	72 (72.7)	57 (59.4)	46 (73)	45 (76.3)	733 (64.9)

* Except where indicated otherwise, values are the number (%) of patients. SD: Standard deviation, SLE: Systemic Lupus Erythematosus

** Other participating countries: Costa Rica (31 patients), Bolivia (24 patients), Puerto Rico (22 patients), Guatemala (12 patients), Venezuela (11 patients), Ecuador (9 patients), Paraguay (9 patients), Honduras (7 patients), El Salvador (6 patients), Nicaragua (6 patients), Panama (3 patients), Dominican Republic (2 patients), Cuba (2 patients)

^aNot including corticosteroids and hydroxychloroquine

^bSLE activity was defined as the presence of flares-up diagnosed by a doctor during the previous 6 months

^cCorticosteroid use was defined as use of prednisone ≥ 7.5 mg daily or equivalent during the last month

^dSmoking was defined as currently smoking or having quit < 6 months ago

^eRisk factors for pneumonia assessed were: age > 50 years, diabetes, current use of immunosuppressors, daily dose of prednisone > 7.5 mg or equivalent during the last month, SLE activity, and the coexistence of chronic cardiac, respiratory or renal disease

Table 2 Vaccine coverage and reasons for non-vaccination of Latin American patients*

	Argentina (265)	Mexico (214)	Brazil (190)	Chile (99)	Peru (96)	Colombia (63)	Uruguay (59)	All patients (1130)
Influenza	178 (67.2)	38 (17.8)	114 (60)	51 (51.5)	21 (21.9)	15 (23.8)	19 (32.2)	482 (42.7)
Pneumococcal	146 (55.1)	23 (10.7)	41 (21.6)	14 (14.1)	9 (9.4)	8 (12.7)	14 (23.7)	282 (25)
Influenza and pneumococcal	128 (48.3)	11 (5.1)	35 (18.4)	10 (10.1)	6 (6.3)	5 (7.9)	9 (15.3)	222 (19.6)
Tetanus	129 (48.7)	61 (28.5)	87 (45.8)	9 (9.1)	21 (21.9)	18 (28.6)	50 (84.7)	424 (37.5)
No influenza and no pneumococcal	69 (26)	164 (76.6)	70 (36.8)	44 (44.4)	72 (75)	45 (71.4)	35 (59.3)	588 (52)
Incomplete vaccination ^a	194 (73.2)	205 (95.8)	165 (86.8)	96 (97)	93 (96.9)	61 (96.8)	53 (89.8)	998 (88.3)
Lack of medical prescription ^b	126 (64.9)	135 (63.1)	104 (63)	73 (76)	65 (69.9)	48 (78.7)	27 (50.9)	645 (64.6)
Rejection by patients ^b	26 (13.4)	29 (14.1)	15 (9.1)	9 (9.4)	16 (17.2)	1 (1.6)	15 (28.3)	127 (12.7)
Not available/ cost issues ^b	18 (9.3)	13 (6.3)	21 (12.7)	9 (9.4)	12 (12.9)	5 (8.2)	1 (1.9)	113 (11.3)
Others ^b	28 (14.4)	36 (17.6)	31 (18.8)	13 (13.5)	7 (7.5)	9 (14.8)	10 (18.9)	164 (16.4)

* Except where indicated otherwise, values are the number (%) of patients

^aIncludes those who reported not having received at least one of the vaccines (influenza, pneumonia or tetanus)

^bThe percentage was calculated using the number of non-vaccinated as the denominator

≥7.5 mg (or equivalent), this subgroup was analyzed. A total of 1015 (89.6%) met this condition. Of them, 437 (43%) and 259 (25.2%) received the influenza and pneumococcal vaccines respectively. In addition, we analyzed vaccination coverage among not immunosuppressed (115 patients, 10.2%). Of them, 45 (39.1%) and 23 (20%) reported having received the influenza and pneumococcal vaccines respectively. No differences were found regarding vaccination coverage between both groups (influenza coverage: 43% vs 39.1%, *p*-value: 0.42 and pneumococcal coverage: 25.2% vs 20%, *p*-value: 0.20).

Europe

There were 794 participants from Europe. Fifty were excluded because they did not meet inclusion criteria. The majority of patients (95% of the total) were from Spain, Portugal, United Kingdom/Ireland, France and Italy. Data on demographics, risk factors for pneumonia and specific for SLE are shown in Table 3. Like the Latin American participants, the majority were young women with more than 5 years of SLE diagnosis. Almost 75% had two or more risk factors for pneumonia, the most frequent being the use of immunosuppressors / corticosteroids and the activity of SLE. Remarkably, approximately 30% reported being a smoker. Hydroxychloroquine use did not exceed 73% in any of the countries.

Information on vaccination coverage is shown in Table 4. Influenza coverage in the region only reached 49.3%, while for pneumonia it did not exceed 37%. Along the same lines, tetanus coverage was less than 50%. Similar to what was found in Latin America, marked differences were observed between the countries with respect to the vaccination rate. Lack of a medical prescription was the most frequent cause of non-vaccination, although almost 20% did not get vaccinated because of refusal.

As with Latin American patients, vaccine coverage was analyzed in immunosuppressed patients (549, 73.5%) and those who were not (198, 26.5%). Coverage rates for influenza and pneumococcus for immunosuppressed were 53% (291/549) and 39.7% (218/549) respectively, while for non-immunosuppressed were 38.9% (77/198) and 27.8% (55/198). Unlike Latin America, a significant difference was found in the vaccination rate, being greater in immunosuppressed (influenza vaccine: 53% vs 38.9%, *p*-value: 0.000; and pneumococcal vaccine: 39.7% vs 27.8%, *p*-value: 0.003).

Comparison between Latin America and Europe

Comparison between the two regions is shown in Table 5. Statistically significant differences were observed in most of the variables compared although in general they did not reach 10%. Regarding demographics, risk factors for pneumonia and SLE-specific data, the most remarkable differences were average age, mean disease duration, immunosuppressors and hydroxychloroquine use, and the percentage of risk factors. Latin American patients were 5 years younger on average, with shorter mean disease duration, higher percentage of use of immunosuppressors and hydroxychloroquine, while European patients presented a higher percentage of risk factors for pneumonia, the high percentage of smokers being remarkable. In terms of vaccination coverage, Latin American patients had lower coverage for pneumococcus and tetanus, and a higher percentage of unvaccinated patients for both influenza and pneumococcus. Furthermore, vaccination rate in immunosuppressed patients was found to be higher in Europe (influenza coverage: 43% vs 53%, *p*-value: 0.000; and pneumococcal coverage: 25.2% vs 39.7%, *p*-value: 0.000). The most frequent reported cause of non-vaccination in both regions was

Table 3 Demographics, risk factors for pneumonia, and SLE-specific data of European patients *

	Spain (232)	Portugal (184)	UK/Ireland (151)	France (82)	Italy (59)	All patients (744)**
Age, years (SD)	43 (11.1)	42,1 (10.1)	44.5 (11.6)	40,3 (11.2)	42.8 (10.1)	42.7 (11)
Female	220 (94.8)	179 (97.3)	144 (95.4)	79 (96.3)	56 (94.9)	711 (95.6)
Patients > 50 years	60 (25.9)	37 (20.1)	42 (27.8)	13 (15.9)	13 (22)	174 (23.4)
Disease duration, years (range)	10 (1–39)	10 (0–34)	9 (0.5–41)	5 (1–31)	10 (1–37)	9 (0–41)
Disease duration > 7 years	141 (60.8)	109 (59.2)	86 (57)	38 (46.3)	37 (62.7)	426 (57.2)
Immunosuppressors ^a	173 (74.6)	135 (73.4)	102 (67.5)	67 (81.7)	43 (72.9)	546 (73.4)
SLE activity ^b	119 (51.3)	94 (51.1)	88 (58.3)	45 (54.9)	30 (50.8)	395 (53.1)
Corticosteroid use ^c	70 (30.2)	81 (44)	40 (26.5)	26 (31.7)	23 (39)	249 (33.5)
Hydroxychloroquine	152 (65.5)	129 (70.1)	109 (72.2)	44 (53.7)	31 (52.5)	492 (66.1)
Smoking ^d	70 (30.2)	61 (33.2)	29 (19.2)	29 (35.4)	22 (37.3)	219 (29.4)
Chronic renal disease	42 (18.1)	16 (8.7)	17 (11.3)	8 (9.8)	14 (23.7)	104 (14)
Chronic respiratory disease	35 (15.1)	22 (12)	33 (21.9)	18 (22)	9 (15.3)	124 (16.7)
Chronic cardiac disease	22 (9.5)	18 (9.8)	8 (5.3)	4 (4.9)	6 (10.2)	64 (8.6)
Diabetes	6 (2.6)	6 (3.3)	3 (2.0)	2 (2.4)	2 (3.4)	20 (2.7)
> 1 risk factors for pneumonia ^e	172 (74.1)	140 (76.1)	113 (74.8)	57 (69.5)	47 (79.7)	556 (74.7)

* Except where indicated otherwise, values are the number (%) of patients. SD: Standard deviation, SLE: Systemic Lupus Erythematosus

** Other participating countries: Belgium (12 patients), Netherlands (6 patients), Luxembourg (4 patients), Denmark (3 patients), Germany (2 patients), Greece (2 patients), Switzerland (2 patients), Andorra (1 patient), Croatia (1 patient), Cyprus (1 patient), Iceland (1 patient), Norway (1 patient)

^aNot including corticosteroids and hydroxychloroquine

^bSLE activity was defined as the presence of flares-up diagnosed by a doctor during the previous 6 months

^cCorticosteroid use was defined as use of prednisone ≥ 7.5 mg daily or equivalent during the last month

^dSmoking was defined as currently smoking or having quit < 6 months ago

^eRisk factors for pneumonia assessed were: age > 50 years, diabetes, current use of immunosuppressors, daily dose of prednisone > 7.5 mg or equivalent during the last month, SLE activity, and the coexistence of chronic cardiac, respiratory or renal disease

lack of medical prescription, with no statistically significant difference between the two regions. Statistically significant differences, although small, were observed in the percentage of non-vaccination due to cost/accessibility, being more frequent in Latin America, while in Europe refusal to be vaccinated was more frequent.

Factors associated with vaccination coverage

Latin America

Analysis of the factors associated with vaccination coverage is shown in Table 6. Initial analysis found that history of chronic renal disease, age > 50 years, and tetanus coverage were associated with vaccination. The multivariate analysis showed that all three factors mentioned

Table 4 Vaccine coverage and reasons for non-vaccination of European patients*

	Spain (232)	Portugal (184)	UK/Ireland (151)	France (82)	Italy (59)	All patients (744)
Influenza	116 (50)	79 (42.9)	112 (74.2)	26 (31.7)	13 (22)	367 (49.3)
Pneumococcal	72 (31)	53 (28.8)	74 (49)	47 (57.3)	8 (13.6)	271 (36.4)
Influenza and pneumococcal	59 (25.4)	38 (20.7)	69 (45.7)	21 (25.6)	5 (8.5)	202 (27.2)
Tetanus	84 (36.2)	123 (66.8)	66 (43.7)	53 (64.6)	18 (30.5)	366 (49.2)
No influenza and no pneumococcal	103 (44.4)	90 (48.9)	34 (22.5)	30 (36.6)	37 (62.7)	308 (41.4)
Incomplete vaccination ^a	202 (87.1)	174 (94.6)	113 (74.8)	67 (81.7)	56 (94.9)	620 (83.3)
Lack of medical prescription ^b	143 (70.8)	99 (56.9)	76 (67.3)	25 (37.3)	34 (60.7)	392 (63.2)
Rejection by patients ^b	26 (12.9)	25 (14.4)	17 (15)	27 (40.3)	12 (21.4)	114 (18.4)
Not available/ cost issues ^b	7 (3.5)	5 (2.9)	10 (8.8)	3 (4.5)	1 (1.8)	26 (4.2)
Others ^b	34 (16.8)	29 (16.7)	15 (13.3)	15 (22.4)	9 (16.1)	110 (17.7)

* Except where indicated otherwise, values are the number (%) of patients

** Other participating countries: Belgium (12 patients), Netherlands (6 patients), Luxembourg (4 patients), Denmark (3 patients), Germany (2 patients), Greece (2 patients), Switzerland (2 patients), Andorra (1 patient), Croatia (1 patient), Cyprus (1 patient), Iceland (1 patient), Norway (1 patient)

^aIncludes those who reported not having received at least one of the vaccines (influenza, pneumonia or tetanus)

^bThe percentage was calculated using the number of non-vaccinated as the denominator

Table 5 Comparison between Latin American and European patients *

	Latin America (1130)	Europe (744)	Difference (95% CI)	P Value
Age, years (SD)	37.9 (11.3)	42.7 (11)	4.8 (3.8–5.9)	< 0.001
Female	1096 (97)	711 (95.6)	1.4 (–0.3–3.4)	0.13
Patients > 50 years	171 (15.1)	174 (23.4)	8.2 (4.6–12)	< 0.001
Disease duration > 7 years	525 (46.5)	426 (57.2)	10.8 (6.2–15.3)	< 0.001
Immunosuppressors ^a	972 (86)	546 (73.4)	12.6 (8.9–16.4)	< 0.001
SLE activity ^b	674 (59.6)	395 (53.1)	6.6 (2.0–11.1)	0.004
Corticosteroid use ^c	445 (39.4)	249 (33.5)	5.9 (1.5–10.3)	0.009
Hydroxychloroquine	858 (75.9)	492 (66.1)	9.8 (5.6–14.0)	< 0.001
Smoking ^d	209 (18.5)	219 (29.4)	10.9 (7–14.9)	< 0.001
Chronic renal disease	202 (17.9)	104 (14)	3.9 (0.5–7.2)	0.02
Chronic respiratory disease	149 (13.2)	124 (16.7)	3.5 (0.2–6.9)	0.04
Chronic cardiac disease	110 (9.7)	64 (8.6)	1.13 (–1.6–3.7)	0.39
Diabetes	72 (6.4)	20 (2.7)	3.7 (1.8–5.5)	< 0.001
> 1 risk factors for pneumonia ^e	733 (64.9)	556 (74.7)	9.9 (5.6–14.0)	< 0.001
Influenza	482 (42.7)	367 (49.3)	6.7 (2.1–11.3)	0.005
Pneumococcal	282 (25)	271 (36.4)	11.5 (7.2–15.7)	< 0.001
Influenza and pneumococcal	222 (19.6)	202 (27.2)	7.5 (3.6–11.5)	< 0.001
Tetanus	424 (37.5)	366 (49.2)	11.7 (7.1–16.2)	< 0.001
No influenza and no pneumococcal	588 (52)	308 (41.4)	10.6 (6.0–15.2)	< 0.001
Incomplete vaccination ^f	998 (88.3)	620 (83.3)	5.0 (1.8–8.3)	0.002
Lack of medical prescription ^g	645 (64.6)	392 (63.2)	1.4 (–3.4–6.2)	0.06
Rejection by patients ^g	127 (12.7)	114 (18.4)	5.7 (2.1–9.4)	0.007
Not available/ cost issues ^g	113 (11.3)	26 (4.2)	7.1 (4.5–9.6)	< 0.001
Others ^g	164 (16.4)	110 (17.7)	1.3 (–5.2–2.4)	0.90

* Except where indicated otherwise, values are the number (%) of patients. SD: Standard deviation, SLE: Systemic Lupus Erythematosus

^aNot including corticosteroids and hydroxychloroquine

^bSLE activity was defined as the presence of flares-up diagnosed by a doctor during the previous 6 months

^cCorticosteroid use was defined as use of prednisone ≥ 7.5 mg daily or equivalent during the last month

^dSmoking was defined as currently smoking or having quit < 6 months ago

^eRisk factors for pneumonia assessed were: age > 50 years, diabetes, current use of immunosuppressors, daily dose of prednisone > 7.5 mg or equivalent during the last month, SLE activity, and the coexistence of chronic cardiac, respiratory or renal disease

^fIncludes those who reported not having received at least one of the vaccines (flu, pneumonia or tetanus)

^gThe percentage was calculated using the number of non-vaccinated as the denominator

were positively associated with influenza coverage (chronic renal disease: OR = 1.38, 95% CI = 1.01–1.88, p value = 0.044; age > 50 years: OR = 1.70, 95% CI = 1.22–2.37, p value = 0.002; and tetanus coverage: OR = 2.25, 95% CI = 1.75–2.88, p value < 0.001) and pneumococcal (chronic kidney disease: OR = 2.30, 95% CI = 1.63–3.35, p value < 0.001; age > 50 years: OR = 1.67, 95% CI = 1.15–2.42, p value = 0.007; and tetanus coverage: OR = 3.79, 95% CI = 2.85–5.05, p value < 0.001). Thus, tetanus coverage was the most important factor associated with coverage of both vaccines.

Europe

The analysis is shown in Table 6. The univariate analysis found an association between history of chronic respiratory disease, smoking, use of immunosuppressors, age >

50 years, and tetanus coverage with vaccination coverage. Multivariate analysis showed that immunosuppression and tetanus coverage were positively associated with influenza coverage (OR = 1.97, 95% CI = 1.40–2.77, p value < 0.001 and OR = 1.54, 95% CI = 1.14–2.07, p value = 0.005 respectively) and pneumococcus (OR = 1.85, 95% CI = 1.27–2.70, p value 0.001 and OR 3.91, 95% CI 2.83–5.40, p value < 0.001 respectively), while smoking was negatively associated with both (coverage for influenza: OR 0.55, 95% CI 0.39–0.76, p value < 0.001; and coverage for pneumococcus: OR = 0.67, 95% CI = 0.47–0.96, p value = 0.029). Multivariate analysis also showed that age > 50 years was positively associated with coverage for influenza (OR = 2.37, 95% CI = 1.65–3.41, p value < 0.001), while history of chronic respiratory disease was associated with coverage for pneumococcus (OR = 1.86,

Table 6 Factors associated with vaccination coverage*

	Influenza coverage				Pneumococcal coverage			
	Initial analysis		Adjusted model ^a		Initial analysis		Adjusted model ^a	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Latin America								
Chronic renal disease	1.30 (0.96–1.77)	0.089	1.38 (1.01–1.88)	0.044	2.00 (1.44–2.77)	< 0.001	2.30 (1.63–3.35)	< 0.001
Age > 50 years	1.69 (1.22–2.35)	0.001	1.70 (1.22–2.37)	0.002	1.63 (1.15–2.32)	0.006	1.67 (1.15–2.42)	0.007
Tetanus coverage	2.24 (1.75–2.86)	< 0.001	2.25 (1.75–2.88)	< 0.001	3.62 (2.74–4.80)	< 0.001	3.79 (2.85–5.05)	< 0.001
Europe								
Chronic respiratory disease	NS ^d	NS ^d			1.73 (1.18–2.56)	0.006	1.86 (1.23–2.82)	< 0.001
Smoking ^b	0.57 (0.42–0.79)	0.001	0.55 (0.39–0.76)	< 0.001	0.72 (0.52–1.01)	0.058	0.67 (0.47–0.96)	0.029
Immunosuppressors ^c	1.77 (1.27–2.47)	0.001	1.97 (1.40–2.77)	< 0.001	1.71 (1.20–2.44)	0.003	1.85 (1.27–2.70)	< 0.001
Age > 50 years	2.16 (1.53–3.08)	< 0.001	2.37 (1.65–3.41)	< 0.001	NS ^d	NS ^d		
Tetanus coverage	1.45 (1.08–1.93)	0.012	1.54 (1.14–2.07)	0.005	3.74 (2.72–5.14)	< 0.001	3.91 (2.83–5.40)	< 0.001

* Statistical significance was set at p value < 0.05

^aOnly variables that were significant in the univariate analysis ($p < 0.10$) were included

^bSmoking was defined as currently smoking or having quit < 6 months ago

^cNot including corticosteroids and hydroxychloroquine

^dNot significant

95% CI = 1.23–2.82, p value = 0.003). As in Latin America, tetanus coverage was an important factor associated with vaccination.

Discussion

To our knowledge, this is the first study on influenza and pneumococcus coverage in SLE with focus on Latin America. We note that the coverage of influenza and pneumococcus in Latin America is very low, especially for the latter. Only Argentina had coverage for influenza and pneumococcus > 50%, while Brazil and Chile only reached this percentage for influenza coverage. The percentage of patients who received both vaccines did not exceed 50% in any country. These results are not surprising when compared to tetanus coverage which is widely used in Latin America. These findings are similar to a study on influenza coverage in a cohort of lupus patients from Brazil, with a value of 46% [13].

As expected, vaccination rate, especially for pneumococcus, was lower than in Europe. Furthermore, there were no significant differences in the reported vaccination rate of immunosuppressed and non-immunosuppressed patients. This is noteworthy considering the strong recommendation for vaccination against influenza and pneumococcus in immunosuppressed patients with SLE. This finding contrasts with Europe, where immunosuppressed patients reported the highest rate of vaccination.

Difference in coverage between Latin American countries has been noted before and has no single explanation. According to reports from the Pan American Health Organization [34], coverage for diphtheria vaccine ranged from 64% in Venezuela to 96% in Chile

during 2018. A recent systematic review [35] found that the main barriers to vaccination reported were adverse socioeconomic factors, a low level of education, lack of awareness of diseases and their vaccines, religious and cultural beliefs. Thus, the different health policies, socioeconomic level and the culture of the countries could be the cause of this great discrepancy. However, our study showed that the percentage of non-vaccination that could be attributed to these causes did not exceed 35%.

Contrary to expectations, cost or accessibility issues were not the main causes of non-vaccination, but rather lack of medical prescription in both Latin America and Europe as previously reported [13–16]. These findings are in line with several studies conducted on the subject. A study in Germany showed that less than 8 and 60% of rheumatologists and general practitioners (GP), respectively, monitored the vaccination status of lupus patients [16]. Similarly, in a survey conducted in Ireland, it was found that 50% of rheumatologists did not evaluate vaccination coverage of patients and less than 45% did so before indicating immunosuppression [36]. Causes for lack of indication for vaccination may include lack of knowledge about vaccination recommendations and concerns about vaccine safety in immunosuppressed hosts [15]. However, several studies suggest that an important cause would be the perceived responsibility of specialists regarding their role in preventive health care. In the Irish work mentioned above, it was observed that more than half of the rheumatologists considered that the responsibility for vaccination was the domain of the GP [36]. Similarly, a survey of rheumatologists on screening for hyperlipidemia in rheumatoid arthritis (RA) showed that the majority did not regard this

practice as their responsibility [37]. In the same line, a study on preventive care of risk factors for cardiovascular disease in RA showed that, although most rheumatologists are aware of the increased risk in these patients, they rarely identify or act to modify them [38]. Thus, patients who are only seen by specialists are less likely to be vaccinated [39]. This would explain the differences in vaccination coverage among Latin American countries: those countries with a good primary care system will have a higher vaccination rate. Similarly, those European countries with a better primary care system are those that would present the highest vaccination rates for pneumococcus and influenza in the region. On the other hand, GP may not be aware of the need for lupus patients to be vaccinated against pneumococcus and influenza, regardless of patient age [15].

For the aforementioned, it is necessary to involve the specialist in vaccination control. Several measures can be useful to improve vaccination control without significantly overloading patient care time. Placing vaccination reminders in specialized care centers has proven to be a cost-effective measure to improve the vaccination rate in patients with rheumatic disease [40]. Automatic reminders in digital medical records would also be another useful measure [12], although not all care centers in Latin America have this technology. For these measures to be useful, it is essential that the specialist and the GP work together, sharing responsibility for the primary prevention of the patient with rheumatic disease.

This study has several limitations. First, the final questionnaire used, in each of the language versions, was a modified and unvalidated version of other questionnaires. Second, self-reported data may overestimate or underestimate true vaccination coverage due primarily to recall bias [19, 41]. Third, diagnosis of SLE was self-referred and could not be verified in a medical record. Fourth, to avoid the respondent's burden we tried to make the questionnaire as short and simple as possible [42]. Socioeconomic situation was evaluated with a single question within the causes of non-vaccination and SLE activity was assessed with a short question rather than using long questionnaires (eg, SLAQ [43]). However, this oversimplification could produce a significant information bias. Fifth, as only those who use the internet and especially social networks participate, there is an important selection bias. Finally, the participation of some countries in the region was low, probably due to the lack of interest of patients in participating. This implies that the sample could be non-representative.

Conclusion

In conclusion, our work shows that there is poor coverage for pneumococcus and influenza in Latin

America, especially compared to regions such as Europe, the main cause being the lack of medical prescription. Health policies are needed that improve coordination between specialists and GPs as well as raise awareness about the importance of preventive health care for lupus patients.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s42358-021-00197-1>.

Additional file 1. Spanish version of the survey questionnaire.

Additional file 2. English version of the survey questionnaire.

Additional file 3. French version of the survey questionnaire.

Additional file 4. Italian version of the survey questionnaire.

Additional file 5. Portuguese version of the survey questionnaire.

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Authors' contributions

ECH and BCO participated in study design and data collection. ECH participated in data analysis. ECH, BCO and CFL participated in drafting of the manuscript. All authors have read and approved the final manuscript.

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Availability of data and materials

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

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Review Board and the Human Research Ethics Committee (Approval ID: DI-2018-553-HGACD), which complied with the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

None.

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