



The COVID-19 epidemic curve and vaccine acceptance among patients with rheumatic diseases: an ecological study

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Abstract

The attitudes toward emerging COVID-19 vaccines have been of great interest worldwide, especially among vulnerable populations such as patients with rheumatic and musculoskeletal diseases (RMDs). The aim of this study was to analyze the relationship between the nationwide number of COVID-19 cases and deaths, and vaccine acceptance or hesitancy of patients with RMDs from four patient care centers in Mexico. Furthermore, we explored differences in acceptance according to specific diagnoses: rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). This ecological study was a secondary analysis of a cross-sectional study using a validated questionnaire to measure vaccine acceptance. We generated a global Likert scale to evaluate overall attitudes toward the COVID-19 vaccine. We analyzed data from 1336 patients from March to September 2021: 85.13% (1169) were women, with a mean age of 47.87 (SD 14.14) years. The most frequent diagnoses were RA (42.85%, 559) and SLE (27.08%, 393). 635(47.52%) patients were unvaccinated, 253(18.93%) had one dose and 478(35.77%) had two doses. Of all participating patients, 94% were accepting toward the COVID-19 vaccine. Vaccine acceptance remained consistently high throughout the study. However, differences in vaccine acceptance are identified when comparing diagnoses. The peak of the national epidemic curve coincided with an increase in hesitancy among patients with RA. Contrastingly, patients with SLE became more accepting as the epidemic curve peaked. Mexican patients show high acceptance of the COVID-19 vaccine, influenced in part by a patient's specific diagnosis. Furthermore, vaccine acceptance increased mirroring the curve of COVID-19 cases and deaths in the country. This should be taken into consideration when updating recommendations for clinical practice.

Keywords COVID-19 vaccine · Rheumatic diseases · Vaccine hesitancy · Vaccine acceptance · COVID-19

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Introduction

The COVID-19 pandemic caused by the SARS-CoV-2 virus has mobilized efforts at an unprecedented scale to develop vaccines and to implement vaccination programs in record time [1–3]. In Mexico, the COVID-19 vaccine allocation strategy has prioritized those most vulnerable to infection, including older adults, persons with associated comorbidities, and immunosuppressed individuals such as patients with rheumatic and musculoskeletal diseases (RMDs). These patients are made vulnerable to infection both by their underlying conditions and, in some cases, by immunomodulatory treatments [3].

The impact of COVID-19 on patients with RMDs is currently being assessed by the international rheumatology community through the COVID-19 Global Rheumatology Alliance [4]. Similarly, expert groups such as the European Alliance of Associations for Rheumatology (EULAR) have published recommendations for the vaccination of patients with RMDs. Generally, vaccination is encouraged for all patients regardless of their rheumatic disease or type of vaccine. There are no general recommendations to change or pause medications when patients receive a vaccine, and modifications should only be considered on a case-by-case basis [5].

In 2019, the World Health Organization declared vaccine hesitancy one of the top 10 threats to global health [6]. This phenomenon is defined as a “delay in acceptance or refusal of vaccination despite availability of vaccination services” [7]. In Mexico, different types and brands of COVID-19 vaccines have been made available throughout the pandemic depending on availability given global vaccine nationalism. Figure 1 illustrates the timeline of the vaccination campaign in Mexico, starting on December 2020, distributed by public health entities. The campaign prioritized frontline health workers and education staff, followed by older adults (60 and over). Afterwards, vaccines were made available in stages, according to descending age ranges and existing vulnerabilities (i.e., pregnancy, comorbidities). The market share was occupied as follows: PfizerBioNTech (December 2020), CanSinoBio (January 2021), Sputnik V (February 2021), AstraZeneca (March 2021), Sinovac (April 2022), Johnson & Johnson (June 2021), Moderna (August 2021), and Abdala (November 2022). This heterogeneity in vaccines has caused some uncertainty about the efficacy and safety of specific vaccines among the general population, potentially generating vaccine hesitancy.

To evaluate the phenomenon of COVID-19 vaccine hesitancy, acceptance, or refusal among the general population in Mexico, researchers at the National Institute of Public Health conducted the nationwide study Ensanut 2020 Covid-19 from August to November 2020, prior to the start of the national vaccination campaign. The study included 10,796 participants: 62.3% reported potential acceptance of the vaccines, 28.2% reported refusal, and 9.5% reported a state of hesitancy [8]. Similar surveys have been conducted in other countries, finding that acceptance rates of the COVID-19 vaccination ranged from 54.9% to 90% in the general population globally [9]. Further studies tried to describe this phenomenon among patients with RMDs specifically. In Mexico, for example, a recent study reported 72.2% acceptance among patients [10]. Meanwhile, vaccine acceptance is 85% for patients in the United States and Italy [11, 12], 65% in Australia [13], 63% in Arab countries [14], 54% in Western India [15] 29.2% in Turkey [16].

In this study, the main objective was to analyze the relationship between vaccine attitudes (acceptance or hesitancy) and the nationwide number of COVID-19 cases and deaths as a proxy for risk perception. Additionally, we aimed to analyze differences in acceptance between patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) as the two most frequent rheumatic diagnoses, and between patients with RMDs from different hospitals in the country.

Materials and methods

An ecological study was conducted as a secondary analysis of a cross-sectional study integrated by aggregate measures of COVID-19 vaccine acceptance among patients with

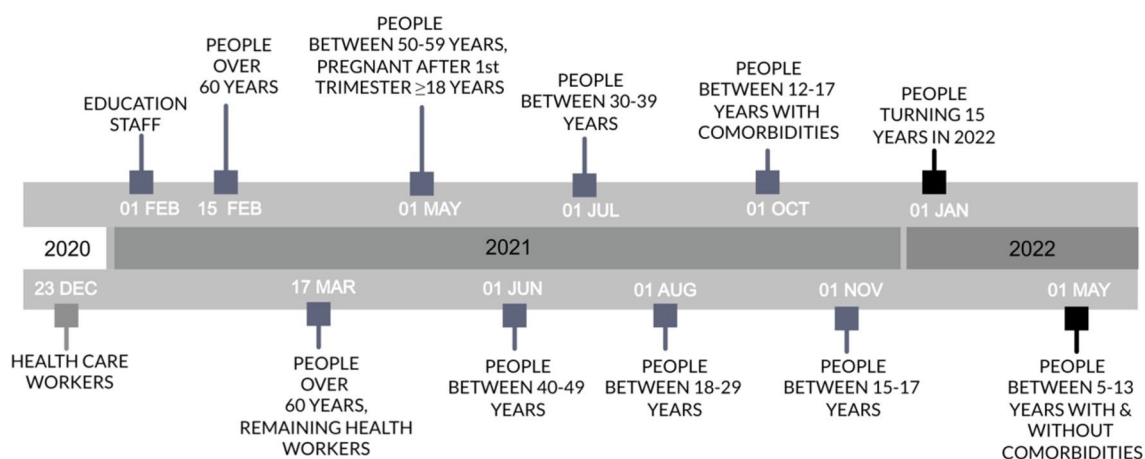


Fig. 1 Timeline of the COVID-19 vaccination campaign in Mexico

Table 1 Comparison of sociodemographic characteristics, rheumatic disease diagnoses, comorbidities, treatment, and COVID-19 vaccination status of patients at different hospitals

	HGCh n(%)	HGM n(%)	HU n(%)	INCMNSZ n(%)	<i>P</i>
Total, <i>n</i> = 1336	292 (21.85)	323 (24.17)	242 (18.11)	509 (38.09)	
Age (years), mean (SD)	49.58 (14.74)	44.92 (13.63)	49.17 (13.96)	47.30 (14.31)	< 0.001
Sex (female)	250 (85.62)	278 (86.07)	198 (81.82)	443 (87.03)	0.307
Marital status					
Married	160 (54.79)	120 (37.15)	164 (67.77)	186 (36.54)	< 0.001
Divorced	28 (9.59)	20 (6.19)	12 (4.96)	61 (11.98)	
Single	64 (21.92)	106 (32.82)	54 (22.31)	186 (36.54)	
Domestic partnership	20 (6.85)	62 (19.20)	4 (1.65)	62 (12.18)	
Widowed	20 (6.85)	15 (4.64)	8 (3.31)	14 (2.75)	
Schooling					
0–6 years	49 (16.96)	64 (20.32)	19 (7.95)	53 (10.43)	< 0.001
7–9 years	76 (26.30)	99 (31.43)	31 (12.97)	100 (19.69)	
10–12 years	55 (19.03)	75 (23.81)	53 (22.18)	120 (23.62)	
13–16 years	57 (19.72)	66 (20.95)	91 (38.08)	142 (27.95)	
17–22 years	50 (17.30)	11 (3.49)	40 (16.74)	92 (18.11)	
23 or more years	2 (0.69)	0 (0.00)	5 (2.09)	1 (0.20)	
Healthcare coverage					
Full coverage services*	180 (61.64)	68 (21.06)	165 (68.18)	116 (22.79)	< 0.001
None	30 (10.27)	252 (78.02)	57 (23.55)	374 (73.48)	
Other	82 (28.08)	3 (0.93)	20 (8.26)	19 (3.73)	
Occupation					
Unemployed	10 (3.42)	16 (4.95)	4 (1.65)	28 (5.50)	< 0.001
Employed	57 (19.52)	79 (24.46)	97 (40.08)	164 (32.22)	
Student	12 (4.11)	13 (4.02)	5 (2.07)	22 (4.32)	
Domestic labor	137 (46.92)	159 (49.23)	90 (37.19)	241 (47.35)	
Retired	28 (9.59)	1 (0.31)	17 (7.02)	10 (1.96)	
Other	48 (16.44)	55 (17.03)	29 (11.98)	44 (8.65)	
Comorbidities					
HBP	39 (13.36)	55 (17.03)	26 (10.74)	155 (30.45)	< 0.001
T2DM	12 (4.11)	25 (7.74)	7 (2.89)	52 (10.22)	
Pulmonary disease	12 (4.11)	11 (3.41)	1 (0.41)	39 (7.66)	
Other	26 (8.9)	17 (5.58)	25 (10.32)	190 (37.33)	
Rheumatic diagnosis					
RA	137 (46.92)	140 (43.34)	124 (51.24)	158 (31.04)	< 0.001
SLE	28 (9.59)	115 (35.60)	37 (15.29)	213 (41.85)	
Gout	6 (2.05)	13 (4.02)	0 (0.00)	4 (0.79)	
SpA	3 (1.03)	20 (6.19)	2 (0.83)	37 (7.27)	
APS	3 (1.03)	2 (0.62)	4 (1.65)	43 (8.45)	
OA	48 (16.44)	0 (0.00)	22 (9.09)	4 (0.79)	
Other**	77 (26.35)	43 (13.32)	71 (29.34)	128 (25.15)	
Treatment					
csDMARDs [†]	198 (67.81)	259 (80.19)	156 (64.46)	314 (65.83)	< 0.001
Glucocorticoids ≤ 10 mg	73 (25.00)	75 (23.22)	68 (28.10)	123 (25.79)	0.614
Glucocorticoids > 10 mg	4 (1.37)	41 (12.69)	0 (0.00)	49 (10.27)	
Immunosuppressants [‡]	19 (6.51)	90 (27.86)	15 (6.20)	174 (36.48)	
Biologic drugs [§]	22 (7.53)	6 (1.86)	23 (9.50)	9 (1.89)	
JAK inhibitors	14 (4.79)	1 (0.31)	5 (2.07)	0 (0.00)	
Opportunity to vaccinate	253 (86.64)	222 (68.73)	239 (98.76)	74 (14.54)	< 0.001
Two vaccine doses	178 (60.96)	87 (26.93)	177 (73.14)	36 (7.07)	< 0.001

Table 1 (continued)

HGCh Hospital General “Dr. Salvador Zubirán”, *HGM* Hospital General de México “Dr. Eduardo Liceaga”, *HU* Hospital Universitario “Dr. José Eleuterio Gonzalez”, *INCMNSZ* Instituto Nacional de Ciencias Médicas y Nutrición “Salvador Zubirán”

*Full coverage services: *IMSS* Mexican Social Security Institute, *INSABI* Institute of Health for Welfare, *ISSSTE* Institute for Social Security and Services for State Workers, *HBP* High Blood Pressure, *T2DM* Type 2 diabetes mellitus, *RA* Rheumatoid arthritis, *SLE* Systemic lupus erythematosus, *SA* Spondyloarthritis, *APS* Antiphospholipid syndrome, *OA* Osteoarthritis

**Mixed connective tissue disease, juvenile idiopathic arthritis, inflammatory myopathies, ankylosing spondylitis, Sjögren’s syndrome and vasculitis

†csDMARDs: Methotrexate, sulfasalazine, leflunomide and antimalarial drugs

‡Immunosuppressants: Azathioprine, mycophenolate, cyclophosphamide

§Biologic drugs: Tumor necrosis factor inhibitors, tocilizumab, rituximab, abatacept

RMDs, as well as the inference of the contextual effect of the national COVID-19 epidemic curve [17].

Population

Patients with RMDs were included from four patient care centers in Mexico: Instituto Nacional de Ciencias Médicas y Nutrición “Salvador Zubirán” (INCMNSZ) and Hospital General de México “Dr. Eduardo Liceaga” (HGM) in Central Mexico, and Hospital Universitario “Dr. José Eleuterio Gonzalez” (HU) and Hospital General “Dr. Salvador Zubirán” (HGCh) in Northern Mexico.

We invited patients with RMDs (rheumatoid arthritis, systemic lupus erythematosus, osteoarthritis, primary Sjögren syndrome, systemic sclerosis, etc.) that were at least 18 years old, and that attended routine follow-up visits at one of the participating hospitals between March and September 2021. Patients gave their informed consent prior to the assessments. Rheumatologists completed complementary questionnaires for each patient, regarding their perception of disease activity control and treatment. Patients with RMDs completed questionnaires related to sociodemographic information and a validated instrument of COVID-19 vaccine hesitancy (COVID-19VHQ). Further details about the study population can be found in the primary study [10, 18].

Data collection

The primary information was captured digitally directly on the LimeSurvey® platform or collected on paper and then transcribed and uploaded. The information was analyzed with the SSEM program [19].

Statistical analysis

The primary study variables included: sociodemographic variables (age, sex, schooling, occupation, marital status, healthcare coverage), diagnosis, treatment, rheumatic disease activity control, comorbidities, COVID-19 vaccine

acceptance, number of COVID-19 vaccine doses received, and risk perception of COVID-19 infection.

COVID-19 vaccine acceptance was measured using the “COVID-19 Vaccine Hesitancy Among Patients with Rheumatic Diseases Questionnaire” (C19VHQ). C19VHQ was adapted for and validated in Mexican patients with RMDs [10], from a scale designed for the UK general population [20]. C19VHQ consists of a seven-item scale that evaluates: vaccine acceptance, desire to receive the vaccine, attitude toward the vaccine, willingness to vaccinate, encouragement for others to vaccinate, and impact of receiving the vaccine. Response options were coded from 1 to 5 using a Likert scale [21]: 1 denoted high acceptance, 2 acceptance, 3 neutral position, 4 hesitancy and 5 high hesitancy. A “Don’t know” option was also provided, which was excluded from scoring (score of 0).

The national number of COVID-19 cases and deaths for the same period of the study was obtained from the Mexican Secretariat of Health and was also included in the analysis [22].

Descriptive statistics were used to analyze each of the seven items in the questionnaire, by date, by hospital, and by rheumatic disease. Comparisons between hospitals were made using the Chi-squared test for categorical variables and the Kruskal–Wallis test for continuous variables.

The seven items were grouped into a global Likert scale to measure vaccine acceptance. Patients were classified as accepting when they endorsed four or more of the seven items with a clear positive response (rating of 1–2).

Two types of heatmaps were generated: (a) to show patient-reported number of COVID-19 vaccine doses, and (b) to show national number of COVID-19 cases and deaths during the questionnaire administration. The correlation of these datapoints with C19VHQ responses was evaluated in 17-day intervals.

The analysis was done for all diagnoses, and for RA and SLE specifically. Incomplete questionnaires were excluded from the analysis.

Table 2 Comparison of vaccine acceptance and risk perception of patients with rheumatic diseases at different hospitals

Hospitals	HGCh n(%)	HGM n(%)	HU n(%)	INCMNSZ n(%)	<i>P</i>
Total, <i>n</i> = 1336	292 (21.85)	323 (24.17)	242 (18.11)	509 (38.09)	
1.-Would you take a COVID-19 vaccine if offered?					0.314
Definitely	200 (68.49)	226 (69.97)	161 (66.53)	364 (71.51)	
Probably	56 (19.18)	53 (16.41)	55 (22.73)	84 (16.50)	
I may or I may not	23 (7.88)	15 (4.64)	14 (5.79)	28 (5.50)	
Probably not	4 (1.37)	14 (4.33)	7 (2.89)	11 (2.16)	
Definitely not	6 (2.05)	10 (3.10)	3 (1.24)	14 (2.75)	
Don't know	3 (1.03)	5 (1.55)	2 (0.83)	8 (1.57)	
2.-There exist different COVID-19 vaccines. I consider that:					<0.001
I will want to get it as soon as possible	186 (63.70)	170 (52.63)	173 (71.49)	240 (47.15)	
I will take it when offered	71 (24.32)	85 (26.32)	39 (16.12)	189 (37.13)	
I'm not sure what I will do	20 (6.85)	42 (13.00)	18 (7.44)	59 (11.59)	
I will put off (delay) getting it	9 (3.08)	12 (3.72)	10 (4.13)	8 (1.57)	
I will refuse to get it	5 (1.71)	7 (2.17)	2 (0.83)	12 (2.36)	
Don't know	1 (0.34)	7 (2.17)	0 (0.00)	1 (0.20)	
3.-I would describe my attitude toward receiving a COVID-19 vaccine as:					<0.001
Very enthusiastic	83 (54.25)	51 (26.15)	67 (51.54)	131 (46.62)	
Pretty positive	139 (47.60)	128 (39.63)	112 (46.28)	228 (44.79)	
Neutral	47 (30.72)	65 (33.33)	44 (33.85)	102 (36.30)	
Quite uneasy	18 (11.76)	68 (34.87)	17 (13.08)	36 (12.81)	
Against it	4 (2.61)	4 (2.05)	2 (1.54)	5 (1.78)	
Don't know	1 (0.65)	7 (3.59)	0 (0.00)	7 (2.49)	
4.-If a COVID-19 vaccine was available, I would:					0.070
Get it as soon as possible	246 (84.25)	260 (80.50)	220 (90.91)	419 (82.32)	
Get it when I have time	21 (7.19)	33 (10.22)	8 (3.31)	36 (7.07)	
Delay getting it	14 (4.79)	12 (3.72)	6 (2.48)	22 (4.32)	
Avoid getting it for as long as possible	7 (2.40)	10 (3.10)	6 (2.48)	12 (2.36)	
Never get it	1 (0.34)	3 (0.93)	1 (0.41)	11 (2.16)	
Don't know	3 (1.03)	5 (1.55)	1 (0.41)	9 (1.77)	
5.-If my family or friends were thinking of getting a COVID-19 vaccination, I would:					0.011
Strongly encourage them	117 (40.07)	127 (39.32)	84 (34.71)	231 (45.38)	
Encourage them	154 (52.74)	157 (48.61)	139 (57.44)	210 (41.26)	
Not say anything to them about it	17 (5.82)	33 (10.22)	16 (6.61)	56 (11.00)	
Ask them to delay getting the vaccination	3 (1.03)	3 (0.93)	1 (0.41)	3 (0.59)	
Suggest that they do not get the vaccination	1 (0.34)	2 (0.62)	0 (0.00)	5 (0.98)	
Don't know	0 (0.00)	1 (0.31)	2 (0.83)	4 (0.79)	
6.-With respect to receiving the vaccine, I would describe myself as:					<0.001
Eager to get a COVID-19 vaccine	126 (43.15)	78 (24.15)	77 (31.82)	149 (29.27)	
Willing to get the COVID-19 vaccine	143 (48.97)	200 (61.92)	150 (61.98)	293 (57.56)	
Not troubled about getting the COVID-19 vaccine	14 (4.79)	28 (8.67)	9 (3.72)	40 (7.86)	
Unwilling to get the COVID-19 vaccine	5 (1.71)	15 (4.64)	6 (2.48)	16 (3.14)	
Against the COVID-19 vaccine	3 (1.03)	1 (0.31)	0 (0.00)	5 (0.98)	
Don't know	1 (0.34)	1 (0.31)	0 (0.00)	6 (1.18)	
7.-Taking a COVID-19 vaccination is:					<0.001
Really important	200 (68.49)	144 (44.58)	165 (68.18)	306 (60.12)	
Important	84 (28.77)	169 (52.32)	72 (29.75)	173 (33.99)	
Neither important nor unimportant	2 (0.68)	3 (0.93)	2 (0.83)	17 (3.34)	
Unimportant	1 (0.34)	6 (1.86)	2 (0.83)	2 (0.39)	
Really unimportant	1 (0.34)	0 (0.00)	0 (0.00)	4 (0.79)	

Table 2 (continued)

Hospitals	HGCh n(%)	HGM n(%)	HU n(%)	INCMNSZ n(%)	<i>P</i>
Don't know	4 (1.37)	1 (0.31)	1 (0.41)	7 (1.38)	
Risk perception: Do you believe you will catch a COVID-19 infection?					
Maybe	41 (14.04)	48 (14.86)	48 (19.83)	88 (17.29)	<0.001
No	93 (31.85)	88 (27.24)	28 (11.57)	75 (14.73)	
Probably not	93 (31.85)	55 (17.03)	46 (19.01)	106 (20.83)	
Probably yes	7 (2.40)	60 (18.58)	13 (5.37)	62 (12.18)	
Yes	2 (0.68)	11 (3.41)	0 (0.00)	7 (1.38)	
Don't know	56 (19.18)	61 (18.89)	107 (44.21)	171 (33.60)	

C19VHQ COVID-19 Vaccine Hesitancy Among Patients with Rheumatic Diseases Questionnaire, *HGCh* Hospital General “Dr. Salvador Zubirán”, *HGM* Hospital General de México “Dr. Eduardo Liceaga”, *HU* Hospital Universitario “Dr. José Eleuterio Gonzalez”, *INCMNSZ* Instituto Nacional de Ciencias Médicas y Nutrición “Salvador Zubirán”

Results

A total of 1500 patients with RMDs participated in the survey; 1,366 were selected according to the criteria for completeness. Of these, 85.13% (1,169) were women, with a mean age of 47.87 years (SD 14.14), and a mean of 11.93 years of schooling (SD 4.52). The most frequent diagnoses were RA (42.85%, 559) and SLE (27.08%, 393), and the most frequent comorbidity was High Blood Pressure (HBP) in 18.20% (275) of patients.

Table 1 shows the comparison between hospitals of sociodemographic, clinical and vaccine-related variables. With the exception of sex and glucocorticoid (≤ 10 mg) use, all evaluated variables were statistically significant ($p < 0.001$, highlighted in bold) between hospitals.

Comparisons between patients according to how many COVID-19 doses they had received are shown in Table 2. Statistically significant differences ($p < 0.001$, highlighted in bold) were found for the following variables: hospital, age, HBP as a comorbidity, and RA or SLE diagnosis.

In Table 3, we describe the responses to C19VHQ between hospitals, as well as risk perception of COVID-19 infection. Items 2, 3, 6 and 7 of the questionnaire were the only ones with statistically significant differences ($p < 0.001$, highlighted in bold). Risk perception was low for patients from any hospital, when patients were asked if they believed they would catch a COVID-19 infection.

Considering the number of patients who expressed a positive response (scores of 1–2) in at least four of the seven items in C19VHQ, we determined that 94% of patients with RMDs accept the COVID-19 vaccine. It's worth noting that 90% of patients who had had the opportunity to receive a vaccine at the time of their participation in the study, had chosen to get vaccinated.

Figure 2 depicts the responses of three groups: total population of patients with RMDs (2A), and patients with RA (2B) and SLE (2C) specifically. For visualization

purposes, responses are graphed in 17-day intervals. Graphs illustrate the global Likert scale generated to measure vaccine acceptance (high acceptance, acceptance, neutral, hesitancy, and high hesitancy). Figure 2D depicts heatmaps showing the average number of COVID-19 cases (column 1) and deaths (column 2) in Mexico during the study. The peak of the national epidemic curve (higher numbers of cases and deaths) occurred from end of July to September, as highlighted with bolded text.

Irrespective of the diagnosis (2A), we observed that vaccine acceptance remained constant throughout the study, regardless of the course of the pandemic. However, patterns of acceptance differed for specific diagnoses. The peak of the national epidemic curve coincided with an increase in the endorsement of hesitancy responses by patients with RA, who had higher acceptance on previous dates (2B). In contrast, patients with SLE were initially more hesitant and became more accepting as the national epidemic curve peaked (2C).

Heatmaps in 2A–2C depict the number of participants who had received one or two COVID-19 vaccine doses in each period. The largest number of vaccinated patients coincided with the national epidemic curve peak (July to September) for total patients with RMDs and for specific diagnoses, despite the different patterns of vaccine acceptance described above.

Discussion

In this study, we found a higher vaccine acceptance rate among Mexican patients with RMDs using a Likert scale (94%), compared to previous reports for both the global and national general population and patients with RMDs in other countries [11–16]. High acceptance coincided with the high number of participants who had chosen to receive one or two doses of a COVID-19 vaccine at the time of

Table 3 Comparison of hospitals, ages, comorbidities, rheumatic disease diagnoses and vaccine acceptance of patients according to COVID-19 vaccine doses

	Unvaccinated <i>N</i> <i>n</i> (%)	One dose <i>n</i> (%)	Two doses <i>n</i> (%)	<i>P</i>
Total, <i>n</i> = 1336	635 (47.52)	253 (18.93)	478 (35.77)	
Hospital				
HGCh (292)	57 (8.98)	57 (22.53)	178 (37.24)	< 0.001
HGM (323)	122 (19.21)	114 (45.06)	87 (18.20)	
HU (242)	13 (2.05)	52 (20.55)	177 (37.03)	
INCMNSZ (509)	443 (69.76)	30 (11.86)	36 (7.53)	
Age (years), mean (SD)	43.15 (14.48)	44.83 (10.83)	54.85 (12.62)	< 0.001
Comorbidities				
HBP	165 (25.98)	30 (11.86)	80 (16.74)	< 0.001
Rheumatic diagnosis				
RA	211 (33.23)	121 (47.83)	227 (47.49)	< 0.001
SLE	260 (40.94)	67 (26.48)	66 (13.81)	< 0.001
C19VHQ				
1.-Would you take a COVID-19 vaccine if offered?				
Definitely	425 (66.93)	172 (67.98)	354 (74.06)	0.269
Probably	126 (19.84)	49 (19.37)	73 (15.27)	
I may or I may not	34 (5.35)	19 (7.51)	27 (5.65)	
Probably not	20 (3.15)	5 (1.98)	11 (2.30)	
Definitely not	20 (3.15)	4 (1.58)	9 (1.88)	
Don't know	10 (1.57)	4 (1.58)	4 (0.84)	
2.-There exist different COVID-19 vaccines. I consider that:				
I will want to get it as soon as possible	277 (43.62)	150 (59.29)	342 (71.55)	< 0.001
I will take it when offered	235 (37.01)	56 (22.13)	93 (19.46)	
I'm not sure what I will do	76 (11.97)	33 (13.04)	30 (6.28)	
I will put off (delay) getting it	28 (4.41)	7 (2.77)	4 (0.84)	
I will refuse to get it	17 (2.68)	3 (1.19)	6 (1.26)	
Don't know	2 (0.31)	4 (1.58)	3 (0.63)	
3.-I would describe my attitude toward receiving a COVID-19 vaccine as:				
Very enthusiastic	130 (20.47)	58 (22.92)	144 (30.13)	< 0.001
Pretty positive	271 (42.68)	107 (42.29)	229 (47.91)	
Neutral	151 (23.78)	43 (17.00)	64 (13.39)	
Quite uneasy	63 (9.92)	42 (16.60)	34 (7.11)	
Against it	8 (1.26)	2 (0.79)	5 (1.05)	
Don't know	12 (1.89)	1 (0.40)	2 (0.42)	
4.-If a COVID-19 vaccine was available, I would:				
Get it as soon as possible	484 (76.22)	213 (84.19)	448 (93.72)	< 0.001
Get it when I have time	58 (9.13)	25 (9.88)	15 (3.14)	
Delay getting it	25 (3.94)	5 (1.98)	5 (1.05)	
Avoid getting it for as long as possible	39 (6.14)	6 (2.37)	9 (1.88)	
Never get it	16 (2.52)	0 (0.00)	0 (0.00)	
Don't know	13 (2.05)	4 (1.58)	1 (0.21)	
5.-If my family or friends were thinking of getting a COVID-19 vaccination, I would:				
Strongly encourage them	252 (39.69)	94 (37.15)	213 (44.56)	< 0.001
Encourage them	271 (42.68)	139 (54.94)	250 (52.30)	
Not say anything to them about it	95 (14.96)	16 (6.32)	11 (2.30)	
Ask them to delay getting the vaccination	7 (1.10)	1 (0.40)	2 (0.42)	
Suggest that they do not get the vaccination	6 (0.94)	1 (0.40)	1 (0.21)	

Table 3 (continued)

	Unvaccinated <i>N</i>	One dose <i>n</i> (%)	Two doses <i>n</i> (%)	<i>P</i>
Don't know	4 (0.63)	2 (0.79)	1 (0.21)	
6.-With respect to receiving the vaccine, I would describe myself as:				
Eager to get a COVID-19 vaccine	151 (23.78)	85 (33.60)	194 (40.59)	< 0.001
Willing to get the COVID-19 vaccine	373 (58.74)	150 (59.29)	263 (55.02)	
Not troubled about getting the COVID-19 vaccine	68 (10.71)	11 (4.35)	12 (2.51)	
Unwilling to get the COVID-19 vaccine	30 (4.72)	7 (2.77)	5 (1.05)	
Against the COVID-19 vaccine	7 (1.10)	0 (0.00)	2 (0.42)	
Don't know	6 (0.94)	0 (0.00)	2 (0.42)	
7.-Taking a COVID-19 vaccination is:				
Really important	335 (52.76)	150 (59.29)	330 (69.04)	< 0.001
Important	257 (40.47)	97 (38.34)	144 (30.13)	
Neither important nor unimportant	21 (3.31)	3 (1.19)	0 (0.00)	
Unimportant	7 (1.10)	2 (0.79)	2 (0.42)	
Really unimportant	5 (0.79)	0 (0.00)	0 (0.00)	
Don't know	10 (1.57)	1 (0.40)	2 (0.42)	
Risk perception: Do you believe you will catch a COVID-19 infection?				
Maybe	114 (17.95)	40 (15.81)	71 (14.85)	< 0.001
No	113 (17.80)	55 (21.74)	116 (24.27)	
Probably not	120 (18.90)	67 (26.48)	113 (23.64)	
Probably yes	86 (13.54)	22 (8.70)	34 (7.11)	
Yes	10 (1.57)	7 (2.77)	3 (0.63)	
Don't know	114 (17.95)	40 (15.81)	71 (14.85)	

C19VHQ COVID-19 Vaccine Hesitancy Among Patients with Rheumatic Diseases Questionnaire, *HGCh* Hospital General “Dr. Salvador Zubirán”, *HGM* Hospital General de México “Dr. Eduardo Liceaga”, *HU* Hospital Universitario “Dr. José Eleuterio Gonzalez”, *INCMNSZ* Instituto Nacional de Ciencias Médicas y Nutrición “Salvador Zubirán”, *HBP* High blood pressure, *RA* Rheumatoid arthritis, *SLE* Systemic lupus erythematosus

the study. Contrastingly, other studies have reported lower numbers of vaccinated RMD patients (61.8%), coinciding with higher hesitancy measured by similar questionnaires [23].

This phenomenon of acceptance could be influenced by different factors. First, the “vaccination culture” and confidence toward vaccines that have been historically promoted to the general population by the health sector in Mexico [24]. Second, for patients with RMDs specifically, during the initial phases of the vaccination campaigns, both patients and rheumatologists made a strategic effort to spread information and recommendations about receiving the COVID-19 vaccine [25], including through digital communication and telemedicine [26], taking into consideration previous guidance about the annual influenza vaccine established by rheumatology associations and colleges in the country [27]. The effect of these cultural and historical factors on vaccine attitudes should be further studied in future. The higher acceptance rates observed in patients with SDRs in Mexico compared to other countries could also be explained by the different timing at which

these studies were conducted, considering the preliminary data about vaccine efficacy and safety available at said moments.

Discrepancies in vaccination rates can be partly explained by availability according to the different stages of the national vaccination campaign (as shown in Fig. 1) when the questionnaire was administered at each institution. For example, patients with RMDs from INCMNSZ were invited to participate in this study when the campaign was just starting with older adults. Importantly, most of the participating patients with RMDs were in their 40 s, and therefore were not eligible for vaccination at the beginning of the campaign.

It must be noted that complete refusal of the vaccine was low in the study population, and the majority of those who expressed hesitancy did not consistently endorse the strongest negative responses throughout the C19VHQ. These observations of the high variability of responses demonstrate that selecting a cut-off point to binarize the population between “accepting” and “refusing” can be misleading. Alternatively, a global Likert scale like the one developed

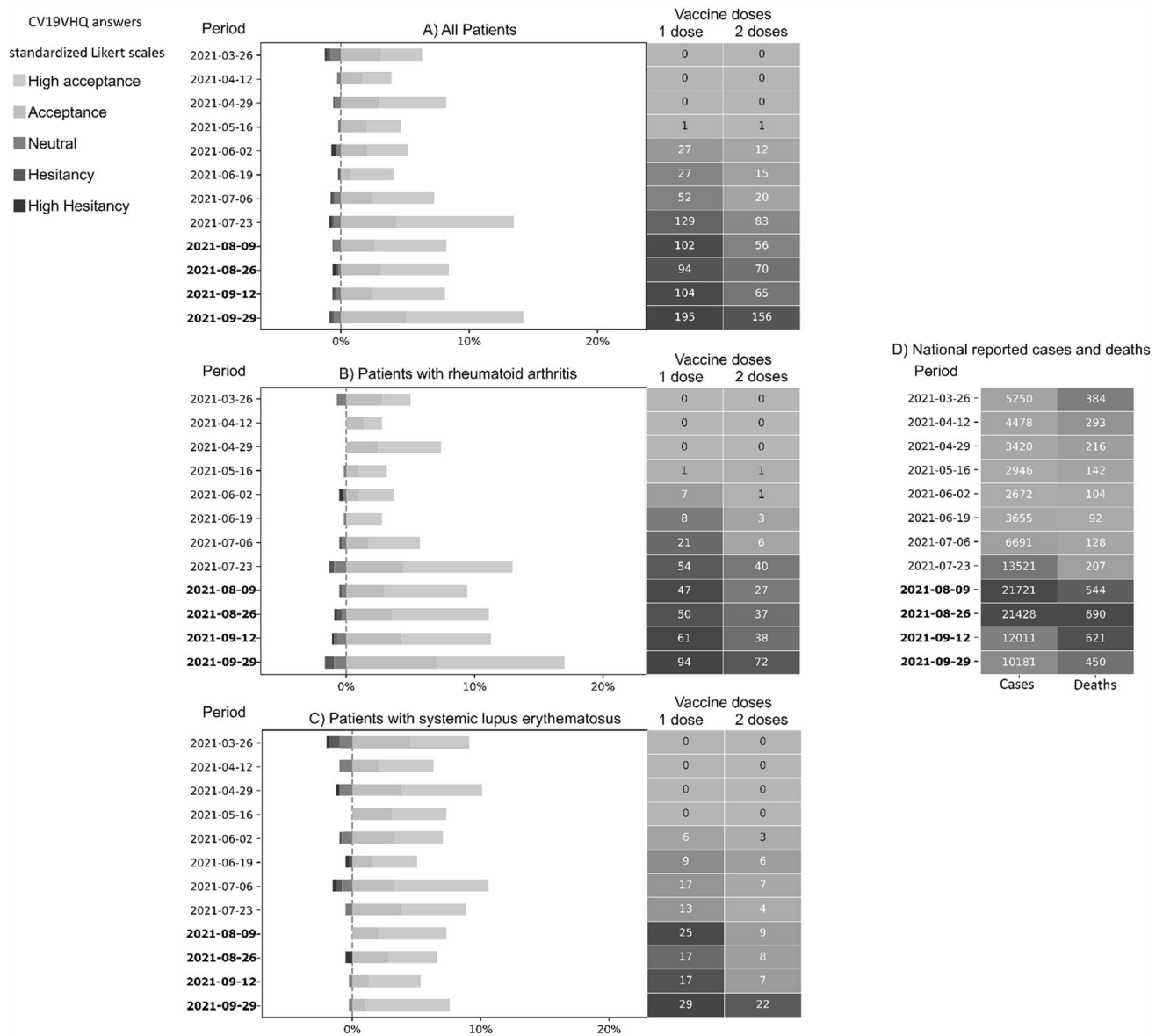


Fig. 2 COVID-19 vaccine acceptance in patients with rheumatic diseases, and with rheumatoid arthritis and systemic lupus erythematosus specifically. Diverging bar charts illustrate the global Likert scale used to measure vaccine acceptance (left of zero), and hesitancy

(right of zero). Heatmaps in **A–C** show the number of vaccinated patients with one or two doses at each 17-day interval. Heatmap **D** shows national epidemiological trends by number of COVID-19 cases and deaths in Mexico. Bolded dates denote the pandemic peak

in this study, which considers the different categories, can more accurately represent the data without over-segmenting the population or overestimating vaccine refusal.

Interestingly, though we found a constant pattern of high vaccine acceptance when evaluating all patients together, differences can be identified when disaggregating diagnoses. Patients with SLE reported more hesitancy at the beginning stages of the study, coinciding with the start of the national vaccination campaign, but became more accepting in times when the number of cases and deaths were highest. In contrast, patients with RA displayed an opposite trend of

acceptance, with the pandemic peak leading to more hesitancy. A possible explanation of these discrepancies could be the different nature of the conditions and the patients’ understanding of them. For example, patients with SLE have been highlighted as a group with reservations and caution, possibly due to general doubts about vaccine safety considering their immunocompromised state and the involvement of the immune system in vaccination [28]. These doubts may then become less pressing when risk perception is higher, leading to a change in attitude toward the need for a vaccine. Acceptance regardless of fear is consistent with other

studies, which have reported a decrease in hesitancy from 2021 to 2022 despite increase in concerns over long-term safety of vaccines [29].

One of the major strengths of this study is that it was conducted using a validated instrument in person during the medical consultation, unlike studies in other countries where vaccine acceptance was evaluated through open virtual/digital questionnaires in social networks or online survey platforms [11, 13, 30, 31], or which have focused solely on physician-reported registries [32]. This has allowed us to describe the phenomenon of acceptance more precisely and accurately in Mexican patients with RMDs, taking into consideration information reported by both the patients and their rheumatologists [33].

One potential limitation is the discrepancy between when the study was conducted in each participating institution, and the development of the national vaccination campaign. Furthermore, given the cross-sectional nature of this study, we are unable to establish a causal association between the measured variables.

In conclusion, patients' attitudes relating to vaccine acceptance or hesitancy vary according to the national COVID-19 epidemic curve, represented by number of deaths and cases. Though patients with RMDs as a group show high levels of vaccine acceptance, different attitudes are identified when comparing diagnoses, possibly due to the specific nature of each condition, the patients' understanding of their disease and the risk perception of each particular group. Finally, this study shows high acceptance of an emergency use vaccine among patients with RMDs, which is consistent with historical acceptance of fully approved vaccines.

Additionally, this study has clinical relevance and actionability since the results can be used to update the Mexican guides and recommendations for the management of rheumatic diseases. Similar updates have been previously made by the EULAR [5, 33], which to our knowledge are the only existing guides which include patient participation and preference in their elaboration. Updated guides should consider the fluctuating nature of the pandemic, the appearance of endemic variants, and the need for boosters for the general population and for vulnerable patients. Importantly, the discrepancies shown between diagnoses highlights the importance of specific guidance for different patient populations, taking into consideration their unique concerns and needs, and how their understanding of their conditions affects patients' views of vaccines in general. Improved guides that include the patients' perspectives will be helpful for the rheumatologists' daily clinical practice.

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Declarations

Conflict of interest The authors declare no conflict of interest.

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