

The Prevalence of Hesitancy Against COVID-19 Vaccination in Patients with Chronic Inflammatory Rheumatic Diseases: A Multicenter Study

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Abstract

Objective: This study aimed to evaluate the prevalence of vaccine hesitancy among patients with chronic inflammatory rheumatic diseases (CIRD) in comparison to those with common mechanical pathologies and to explore the factors influencing vaccine hesitancy. **Methods:** This case-control study in Morocco compared patients with chronic inflammatory rheumatic diseases (CIRD) and those with degenerative mechanical pathologies. Data were collected via questionnaires from December 2021 to December 2022, assessing demographics, medical history, and vaccine hesitancy. Differences between groups were assessed using chi-square tests and t-tests. A logistic regression model was used to identify factors associated with vaccine hesitancy. **Results:** One-hundred-fifteen patients with chronic inflammatory rheumatic diseases (CIRD) were included (median age 49 years, 75.7% women). The majority had rheumatoid arthritis (54.9%) and were on biological treatment (63.2%). About 83% were vaccinated against COVID-19, with 70% reporting no post-vaccination adverse events. Vaccine hesitancy was high (68%), primarily due to fear of adverse events (57.1%). Age was negatively associated with reluctance, but no association was found with gender, education, or CIRD type. In the control group (74 patients, median age 59.5 years, 87.8% women), 92% were vaccinated. Vaccine hesitancy was 74.3%, mainly due to fear of adverse events (59.6%). Univariate and multivariate analyses showed a significant negative association between age and vaccine hesitancy (OR = 0.905, p = 0.023), with no associations to gender or education. **Conclusions:** High COVID-19 vaccine hesitancy was observed in both patient groups, mainly due to concerns about side effects, worsening conditions, low trust in the healthcare system, and insufficient information. Age was also a factor, with younger individuals showing higher reluctance. Increasing awareness is essential to build trust and promote vaccination for herd immunity.

Keywords: chronic inflammatory rheumatic diseases (CIRD), COVID-19 pandemic, vaccine.

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INTRODUCTION

The COVID-19 pandemic, which began in late 2019, had a significant impact on global health and economies. To mitigate its spread, public health measures such as social distancing and mask-wearing were implemented. However, adherence to these measures varied, making vaccination a critical tool in controlling the virus [1].

Vaccine hesitancy (VH), defined as the delay or refusal to receive vaccines despite their availability, emerged as a major challenge in achieving widespread immunization. VH is influenced by multiple factors,

including concerns about vaccine safety, misinformation, and levels of trust in healthcare systems. Socioeconomic status and geographic location also play a role, with higher hesitancy often observed in rural and low-income communities due to limited access to reliable information and healthcare services [2, 3].

Attitudes toward vaccination have differed across countries and populations. In some regions, willingness to vaccinate was strongly linked to recommendations from healthcare professionals, while in others, concerns over vaccine safety persisted, particularly among specific demographic groups [4, 5, 6]. In Western countries, factors such as race, income,

and political affiliation contributed to variations in vaccine acceptance [7, 8].

The pandemic underscored the critical role of mass vaccination in public health. However, overcoming vaccine hesitancy requires targeted efforts to improve trust, combat misinformation, and ensure equitable access to vaccines [9, 10].

This study aimed to evaluate the prevalence of vaccine hesitancy among patients with chronic inflammatory rheumatic diseases (CIRD) in comparison to those with common mechanical pathologies and to explore the factors influencing vaccine hesitancy.

MATERIALS AND METHODS

This case-control study was conducted across multiple medical centers and university hospitals in Morocco. It compared two groups of patients:

- **Cases:** Patients diagnosed with chronic inflammatory rheumatic diseases (CIRD), such as rheumatoid arthritis, spondyloarthritis, and undifferentiated chronic inflammatory rheumatism (UCIR).
- **Controls:** Patients with degenerative mechanical pathologies, including osteoarthritis, herniated discs, and scoliosis.

Study Design and Data Collection:

Data collection was carried out from December 2021 to December 2022. Patients were recruited during routine medical consultations and were asked to complete a structured questionnaire assessing:

- Demographic and socioeconomic characteristics
- Medical history and comorbidities
- COVID-19 vaccination status
- Factors influencing vaccine hesitancy, such as concerns about safety, trust in healthcare providers, and exposure to misinformation

To maintain data quality, patients who declined to participate or gave incomplete responses were excluded from the study. Ethical approval was granted

by the appropriate institutional review boards, and all participants gave informed consent.

Statistical Analysis

Statistical analyses were performed using JAMOV software. Descriptive statistics summarized the characteristics of both groups. Differences between cases and controls were assessed using chi-square tests for categorical variables and t-tests (or non-parametric equivalents) for continuous variables.

A univariate analysis was first conducted to identify potential predictors of vaccine hesitancy, including age, gender, socioeconomic status, comorbidities, and trust in healthcare. Variables with p-values < 0.05 were included in a multivariate logistic regression model to determine independent factors associated with vaccine hesitancy. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported for each variable.

RESULTS

One-hundred-fifteen patients with a chronic inflammatory rheumatic disease (CIRD) were included with a median age of 49 years [16-75], the majority (75.7%) of whom were women. Among the population surveyed, 57.3% completed elementary school, 25.7% finished secondary school, and 16.8% pursued higher education. The majority (54.9%) had RA, 34.5% had SpA, and 4.4% had indeterminate CIRD. The majority (63.2%) were on biological treatment (bDMARDs) and 27.2% of patients were on conventional treatment (CsDMARDs). Approximately 83% of patients were vaccinated against COVID-19. Among them, 55% received 2 shots, 39% received 3 shots, 5.2% received 1 shot and 2.1% received 4 shots. Around 70% of patients did not experience any post-vaccination adverse events. The majority of patients (68%) were reluctant to vaccinate, the most common reason being fear of adverse events (57.1%), followed by fear of aggravating underlying comorbidities (24.7%) and lack of information about the vaccine and vaccination (15.6%) (Table 1).

Table 1: Characteristics of the CIRD patients included:

Characteristics	Patients (CIRD) N = 115	Control Group N = 74	P-value
Age* (years)	49 [16–75]	59.5 [25–83]	<0.001
Gender**			
• Female (%)	87 (75.7%)	65 (87.8%)	0.039
Follow-up Hospital**			
• Rabat-Salé (%)	101 (87.8%)	60 (81.1%)	<0.001
• Agadir (%)	13 (11.3%)	3 (4.1%)	
• Others (%)	1 (0.9%)	14 (14.8%)	
Level of Education**			
• Elementary school (%)	65 (57.3%)	45 (60.8%)	0.006
• Secondary school (%)	29 (25.7%)	7 (9.5%)	
• Higher education (%)	19 (16.8%)	22 (29.7%)	
Type of CIRD**			
• RA (%)	64 (56.1%)	-	

• Spondyloarthritis (%)	41 (36%)	-	
• Indeterminate CIRD (%)	9 (7.9%)	-	
Degenerative Pathologies**			
• Arthrosis (%)	-	53 (72.8%)	
• Herniated Disc (%)	-	10 (12.6%)	
• Others (%)	-	11 (14.6%)	
Current Treatment**			
• Symptomatic Treatment (%)	10 (8.8%)	-	<0.001
• bDMARDs (%)	72 (63.2%)	-	
• CsDMARDs (%)	32 (28.1%)	-	
Other Medications**			
• NSAIDs (%)	-	20 (27.4%)	
• Analgesics (%)	-	48 (65.8%)	
• Pregabalin (%)	-	5 (6.8%)	
COVID-19 Vaccination**			
• Vaccinated (%)	82.3%	91.9%	0.083
• Not Vaccinated (%)	17.7%	8.1%	
Number of Doses**			
• None (%)	0	5 (6.9%)	0.112
• 1 Shot (%)	5 (5.2%)	4 (5.6%)	
• 2 Shots (%)	52 (54.2%)	38 (52.8%)	
• 3 Shots (%)	37 (38.5%)	24 (33.3%)	
• 4 Shots (%)	2 (2.1%)	1 (1.4%)	
Vaccine Hesitancy**			
• Reluctant to Vaccinate (%)	72 (66.1%)	52 (74.3%)	<0.001
• Not Reluctant (%)	37 (33.9%)	18 (25.7%)	
Reasons for Hesitancy**			
• False Beliefs (%)	1 (1.3%)	2 (3.8%)	0.003
• Lack of Information (%)	12 (15.6%)	3 (5.8%)	
• Comorbidities Fear (%)	44 (57.1%)	31 (59.6%)	
• Fear of Adverse Effects (%)	19 (24.7%)	7 (13.5%)	

*: Quantitative variables are expressed as mean \pm standard deviation or median (interquartile range).

** : Qualitative variables are expressed as counts (percentages).

A negative association was found between age and reluctance to vaccinate. However, no association

was found between gender, level of education, type of CIRD, and vaccine hesitancy (Table 2).

Table 2: Multivariate analysis of different factors related to vaccine hesitancy:

	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	0.968	0.945-0.992	0.01	0.971	0.945-0.998	0.012
Gender	1.33	0.579-3.07	0.499	1.177	0.445-2.606	0.721
Level of education:						
· Elementary – Higher education	2.28	0.864-6.03	0.096	1.252	0.418-3.747	0.688
· Secondary –Higher education	1.24	0.555-2.79	0.595	0.744	0.303-1.828	0.519
CIRD:						
· Yes– No	0.732	0.374-1.43	0.361	0.510	0.242-1.075	0.077
Type of CRID:						
· Indeterminate CIRD- RA	0.622	0.141-2.73	0.529			
· SpA- RA	2.486	0.978-6.32	0.056			
Current treatment:						
• bDMARDs-NSAIDs	0.56	0.166-1.88	0.347			
• csDMARDs-NSAIDs	0.409	0.108-1.54	0.187			
• Corticoids-NSAIDs	0.75	0.06-9.27	0.823			
• Pregabalin -NSAIDs	1	0.086-11.59	1			
• Symptomatic treatment-NSAIDs	0.661	0.188-2.32	0.518			

Regarding the second group, 74 control patients from various regions of Morocco were included, with a

median age of 59.5 years (range: 25–83). The majority (87.8%) were women. A total of 92% had been

vaccinated against COVID-19: 52.8% received two doses, 33.3% received three doses, and 5.6% and 1.4% received one and four doses, respectively. Notably, 6.9% of patients had not received any doses. Most patients (60-70%) experienced no post-vaccination adverse events. Vaccine reluctance was observed in approximately 74.3% of patients, with the most common reasons being fear of adverse events (59.6%), followed by a lack of trust in health facilities (13.5%) and concern about exacerbating underlying comorbidities (9.6%).

Univariate and multivariate analyses revealed a significant association between age and vaccine hesitancy (OR = 0.905, 95% CI: 0.933–0.998, $p = 0.023$). However, no significant associations were found with gender or educational level.

DISCUSSION

In our study, the prevalence of vaccine hesitancy (VH) was high in both groups, calculated at 66.1% in patients followed for chronic inflammatory rheumatic diseases (CIRD) and 74.3% in the control group.

A study focusing on vaccine hesitancy among patients with rheumatic and musculoskeletal diseases (RMDs) in Lazio, Italy, found that these patients were less willing to receive the COVID-19 vaccine than healthy controls (82.3% of healthy controls vs. 54.9% of RMD patients) [11].

Global vaccine acceptance exhibited significant regional variations, influenced by demographic, cultural, and contextual factors. The highest acceptance rates were observed in Ecuador, Malaysia, Indonesia, and China (>90%), while the lowest were reported in Kuwait, Jordan, Italy, Russia, Poland, the US, and France (<60%) [3].

In Asia, vaccine acceptance varied across countries. In China, 91.3% of adults were willing to vaccinate, with doctor recommendations and vaccine convenience playing key roles [4]. Malaysia reported an 85.4% booster acceptance rate, particularly among younger, urban, and educated populations [5]. In Indonesia, acceptance declined with lower perceived efficacy, though healthcare workers and individuals perceiving a higher risk were more likely to vaccinate [6].

In Europe, the UK had the highest vaccine acceptance, while Italy and France reported the lowest, reflecting cultural and demographic differences [12]. In Spain, confidence remained strong, with 94.8% acceptance among healthcare workers and 86.6% of unvaccinated individuals intending to get vaccinated [7].

In the United States, the average COVID-19 booster uptake was 43.99%, with hesitancy driven by

concerns about side effects and government mistrust [13]. A systematic review found vaccine acceptance ranging from 12% to 91.4%, influenced by gender, income, and race, with lower acceptance among women, minorities, and low-income groups [8].

A global meta-analysis estimated an overall vaccine acceptance rate of 62.79%, with notable regional differences: the highest in Southeast Asia (70.18%) and the lowest in Africa (39.51%) [9].

In our study, the age emerged as the primary factor associated with vaccine hesitancy. However, no significant associations were found with gender, type of CIRD, educational level, or underlying pathology.

Older patients and men with rheumatic and musculoskeletal diseases (RMDs) were more likely to accept the COVID-19 vaccine, likely due to a higher risk of severe illness [11].

Vaccine acceptance was generally higher among older adults, women, and individuals with higher education, while hesitancy was more common among younger populations, those with lower education levels, and individuals not at high risk for COVID-19. Demographic factors such as age, gender, and socioeconomic status significantly influenced vaccination decisions, with men, older individuals, and those with higher education more likely to accept vaccines, whereas certain racial and lower-income groups exhibited greater hesitancy [7,8].

A meta-analysis identified key factors influencing COVID-19 vaccine acceptance in East Africa, including higher education, good vaccine knowledge, positive vaccine attitude, previous COVID-19 infection, and being male. All these factors were significantly associated with higher vaccine acceptance [14].

Seventeen studies identified factors influencing COVID-19 vaccine uptake, with older age, higher education, good health literacy, male gender, urban residence, and higher socioeconomic status linked to higher acceptance [15]. Male sex, age, marital status, high perceived infection risk, past influenza vaccination, and trust in vaccine efficacy or doctors' recommendations were also key factors in immediate vaccine acceptance [3,4]. Conversely, individuals in areas with COVID-19 cases and those concerned about convenience or cost were less likely to accept the vaccine [4].

COVID-19 affects males and females differently, with males more likely to experience severe outcomes. Although the number of cases is similar for both genders, males are almost three times more likely to need intensive care and have a higher risk of death from

COVID-19. This global trend highlights the importance of understanding these gender differences for better clinical care [16].

In China, factors like work exposure to COVID-19, higher infection risk perception, and vaccine information sources influence vaccine confidence. Gender, age, and employment status also play roles in hesitancy [17]. In France, hesitancy is higher among women, the unemployed, and the less educated, while higher risk perception and belief in vaccine benefits increase acceptance. Concerns about safety and efficacy, along with lower intentions in women and older adults, contribute to hesitancy [18].

The most prominent causes of vaccine hesitancy included fear of adverse effects, fear of worsening underlying pathologies, low confidence in health systems, and insufficient information about the vaccine and vaccination process.

Patients with rheumatic and musculoskeletal diseases (RMDs) were primarily hesitant about the COVID-19 vaccine due to concerns about disease-related side effects and distrust in the vaccine [11].

COVID-19 vaccine hesitancy is primarily driven by worries over side effects, safety, and insufficient information. There is also a call for more clinical studies and updates from governments. To increase acceptance, highlighting vaccine safety and reducing restrictions post-vaccination are key factors [5]. People are more likely to accept the vaccine for self-protection, whereas refusal stems from concerns about side effects and safety. Hesitancy is further influenced by issues like vaccine accessibility, distrust in vaccines and healthcare systems, misinformation, and social inequalities [19,20].

Vaccine acceptance is strongly influenced by trust in the vaccine, healthcare providers, and the government. Hesitancy arises from concerns about safety, side effects, and negative beliefs, particularly in ethnic minorities and underserved communities. Trust issues, including mistrust of healthcare systems and past injustices, significantly contribute to vaccine hesitancy. Financial incentives and historical experiences with healthcare institutions can further reduce trust, especially among marginalized groups [15, 21].

To address vaccine hesitancy, it is crucial to rebuild trust in vaccines, healthcare providers, and policymakers through transparent communication, education, and involvement of trusted community leaders. Understanding the historical context, particularly in communities with a history of medical discrimination, is key. Strategies include improving vaccine access by offering it at convenient locations, providing transportation, and educating both the public

and healthcare workers. Efforts should focus on delivering reliable information, demonstrating expertise, and ensuring unbiased messaging to restore trust and increase vaccine uptake, particularly in marginalized communities [19, 21].

This study has some limitations. The sample size was relatively small due to COVID-19-related travel restrictions, which impacted patient recruitment. Additionally, there may be potential selection bias that could have influenced the results. However, the study's multicentric design, including data from multiple centers across Morocco, offers a broader perspective on the diversity of the Moroccan population.

CONCLUSION

High COVID-19 vaccine hesitancy was noted in both patients with inflammatory rheumatism and the control group with mechanical disorders. Concerns primarily focused on potential side effects, worsening of underlying conditions, low trust in the healthcare system, and insufficient information about the vaccine and vaccination process. Additionally, age was identified as a factor influencing vaccine hesitancy, with younger individuals showing higher levels of reluctance. Increasing awareness is crucial to building public trust and emphasizing the importance of vaccination for achieving herd immunity.

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