

Assessment of hesitancy to COVID-19 vaccine in patients with rheumatic arthritis

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Abstract. – OBJECTIVE: The COVID-19 pandemic caused by SARS-CoV-2 in 2019 has greatly impacted global health, leading to high morbidity and mortality rates. Rheumatoid arthritis (RA) patients have faced numerous challenges during the pandemic, including concerns about infection, limited medical resources, and shortages of medication. While vaccination is a crucial strategy against COVID-19, the reasons behind vaccine hesitancy (VH) among people with RA remain largely unexplored.

SUBJECTS AND METHODS: We conducted a cross-sectional, single-arm study in China from July 18 to August 18, 2021. Using a self-administered questionnaire and a convenient sampling method, we investigated vaccine attitudes and VH among RA patients. The questionnaire developed by the investigators was validated by two public health experts and one senior rheumatologist. It covered sociodemographics, disease-related variables, vaccination attitudes, and willingness, etc. We employed Chi-squared and regression analyses to identify factors associated with VH toward COVID-19 vaccination.

RESULTS: A total of 184 RA patients were enrolled in the survey, with 113 (61.41%) expressing unwillingness to be vaccinated. The Chi-squared test revealed significant differences in employment status and related systemic damage ($p < 0.05$). Among the unvaccinated RA patients, 71.68% believed COVID-19 vaccination might impact their disease. Binary and multicollinearity logistic regression analyses showed that the acute stage of RA ($p < 0.001$, OR = -3.165, 95% CI: 0.035 - 0.164) and fear of disease development caused by drug discontinuation during vaccination ($p < 0.001$, OR = -3.591, 95% CI: 0.005 - 0.157) were the restricting factors influencing the COVID-19 vaccine inoculation rate in RA patients.

CONCLUSIONS: The COVID-19 vaccination rate among RA patients in China is low due to limited knowledge, misconceptions, and insufficient promotion. Boosting confidence and understanding of the vaccine's effectiveness and safety is crucial to improve vaccination success.

Key Words:

Rheumatoid arthritis, COVID-19 Vaccination, Vaccine hesitancy.

Introduction

In 2020, the emergence of COVID-19, a novel strain of coronavirus, gave rise to significant public health concerns¹. With the ongoing global COVID-19 pandemic, vaccination has become a fundamental measure in combating the virus. Vaccines are widely regarded as the most effective means of preventing COVID-19 infection². The World Health Organization (WHO) recommends that all eligible adults receive COVID-19 vaccination promptly to acquire immunization protection. The efficacy of the vaccine is directly proportional to the vaccination coverage. Thus, ensuring an adequate vaccine supply is paramount to accelerating immunization efforts. Consequently, countries worldwide have increased their production capacity, leading to the rapid development of COVID-19 vaccines. Extensive research has confirmed the safety and efficacy of various COVID-19 vaccines³⁻⁶.

Unfortunately, numerous studies⁸⁻¹⁰ addressing vaccine hesitancy (VH) have not attained extensive media coverage. VH, defined as the deliberate postponement or outright rejection of vaccination despite its availability, poses a significant global health menace. The World Health Organization (WHO) recognizes VH as one of the top ten worldwide health threats, on par with Ebola and AIDS⁷. VH represents a multifaceted predicament influenced by various factors such as vaccine type, geographical location, and temporal considerations. Noteworthy factors associated with VH encompass the perception of

vaccine redundancy, apprehension regarding vaccination-induced discomfort, anxieties about the vaccine's rapid development, safety, and efficacy, distrust in the pharmaceutical industry's implementation of vaccination strategies, and other related concerns⁸⁻¹⁰. VH may be influenced by determinants such as educational attainment, gender, occupation, and other demographic variables.

Rheumatoid arthritis (RA) is a prevalent autoimmune and inflammatory disorder affecting a significant proportion of the population in China, with prevalence rates ranging from 0.20% to 0.93%, as reported in relevant surveys¹¹. RA patients face a higher susceptibility to severe forms of COVID-19 infection, resulting in increased morbidity and mortality compared to the general population^{12,13}. China has achieved remarkable progress in its vaccination campaign, having administered over 2.16 billion doses of COVID-19 vaccines as of September 15, 2021, establishing itself as a global leader in vaccination efforts¹⁴. A substantial majority of the Chinese population (83.5%) is willing to receive the COVID-19 vaccine, with 64.2% indicating their openness to receiving a domestically-produced vaccine¹⁵.

While there have been numerous studies¹⁶⁻¹⁸ and analyses on COVID-19 vaccination uptake among the general population, there is currently a gap in the literature regarding COVID-19 vaccination among rheumatoid arthritis (RA) patients. It has been recommended that RA patients receive inactivated COVID-19 vaccines during periods of disease stability¹⁹. In order to address this gap in knowledge, we conducted a scoping study to assess the vaccination status of RA patients in China and identify the factors influencing their VH. We performed a cross-sectional survey with the specific objective of collecting data regarding the COVID-19 vaccination status of patients diagnosed with rheumatoid arthritis (RA). Furthermore, we conducted an analysis to identify the factors influencing VH among this population.

Our findings could inform vaccination campaign planning efforts to increase COVID-19 vaccine acceptance among RA patients and potentially contribute to promoting vaccination acceptance globally.

Subjects and Methods

Planning

We utilized a self-designed anonymous questionnaire and conducted an online survey of RA patients using a convenient sampling method. The

questionnaire was based on previous studies²⁰⁻²², and was collected online by the Department of Rheumatology, Futian Rheumatology Hospital, Futian District, Guangdong Province. Participants were recruited through Wen Juan (<https://www.wenjuan.com/>), one of the most widely used online survey tools in China. The platform ensures user anonymity and does not use profiling cookies or allow identification by tracing. The selected participants were RA patients who met the inclusion criteria for sampling and received long-term care in our hospital, where mutual trust between doctors and patients is high. The questionnaire collected demographic information, basic medical history, drugs use, vaccination willingness, actual vaccination status, and other relevant data related to COVID-19 vaccination.

The study included 184 adult patients with RA in China.

Inclusion Criteria

1. The patient was diagnosed with RA by a local senior professional rheumatologist according to the International Standard ICD-10.
2. Age range: 18-59 years old.
3. Being aware of their diagnosis.
4. Having the reading ability, online APP use technology, and text understanding ability.

Exclusion Criteria

1. Participants who refused to cooperate with the investigation.
2. Individuals in critical condition requiring emergency medical treatment.
3. Individuals who do not meet the basic vaccination requirements, such as being ≥ 60 years old.

The study was approved by the Ethics Committee of Futian Rheumatology Hospital, and all participants were informed of the survey's purpose and agreed to keep their personal information strictly confidential. Respondents did not receive any financial compensation or other benefits for completing the online survey.

Survey Design

Validation

Due to the COVID-19 pandemic, conducting a face-to-face study was not possible. Therefore, we developed a questionnaire for a hypothetical vaccination survey. To ensure its quality, we followed the methods used in previous studies²⁰⁻²². In the first phase, we had the questionnaire design reviewed by three specialists, including two public health professors and one rheumatologist. The experts'

agreement rate was $\geq 80\%$, indicating a high level of consensus on the questionnaire's content.

In the second phase, we conducted a pre-test to validate the questionnaire among 28 RA patients. We used principal component analysis (PCA) to test the dimensionality of the results on the survey items. PCA was used to find linear combinations of the original input variables. The first component of PCA explained 61.70% of the variables, and the eigenvalues of the remaining factors were less than 1, indicating that our data were suitable for factor analyses and reliable. The response rate for our questionnaire was 97.2%.

To ensure logical order, objectivity, and neutrality, the questionnaire problems were arranged based on the study's objectives, avoiding any misleading or unnecessary language that could confuse participants. Data collection involved using a structured questionnaire completed online. To ensure the validity of the data, we excluded responses that selected the same answer for more than 2/3 of the questions. The questionnaire underwent pre-testing and optimization before finalization.

All questions in the questionnaire were closed-ended and required participants to select responses using checkboxes, either through single-choice or multiple-choice questions. The questions were designed using a similar 3/5-point Likert scale²³. The scale included quantification of importance (1-very important, 2-relatively important, 3-uncertain, 4-relatively insignificant, and 5-very insignificant), degree of identification (1-very identification, 2-relatively identification, 3-indifference, 4-relatively identification, and 5-very identification), effective degree (1-effective, 2-average, and 3-ineffective), and risk degree (1-minimal risk, 2-small risk, 3-average risk, 4-relatively high risk, and 5-extremely high risk).

Dissemination

All patients who voluntarily participated in this study anonymously provided their data through an online questionnaire survey using the snowball sampling method. To recruit participants, we designed the questionnaire on the internet and shared links or QR codes randomly *via* WeChat application (Tencent Inc., Shenzhen, GD, China), the largest social platform in China. To ensure diverse data samples, we covered different areas of China. Our patient management involved regular contact with a professional rheumatism team through WeChat, where we monitor patients' conditions. Additionally, we also recruited patients offline through face-to-face consultations during outpatient or inpatient visits and project presentations.

Statistical Analysis

SPSS 17.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis to establish a database for data entry, collation, statistical processing, and analysis. The Chi-square test was conducted for the classified data, and logistic regression analyses were performed with whether to receive the COVID-19 vaccine as the dependent variable, $p < 0.05$ indicated that it was statistically significant.

Results

The Situation of RA Patients Vaccinated with COVID-19 Vaccine

In Figure 1 and Table I, we summarized a total of 184 patients with RA. As of August 15, 2021, 71 patients (38.59%) with RA had received a COVID-19 vaccination, while 113 patients (61.41%) had not been vaccinated against COVID-19.

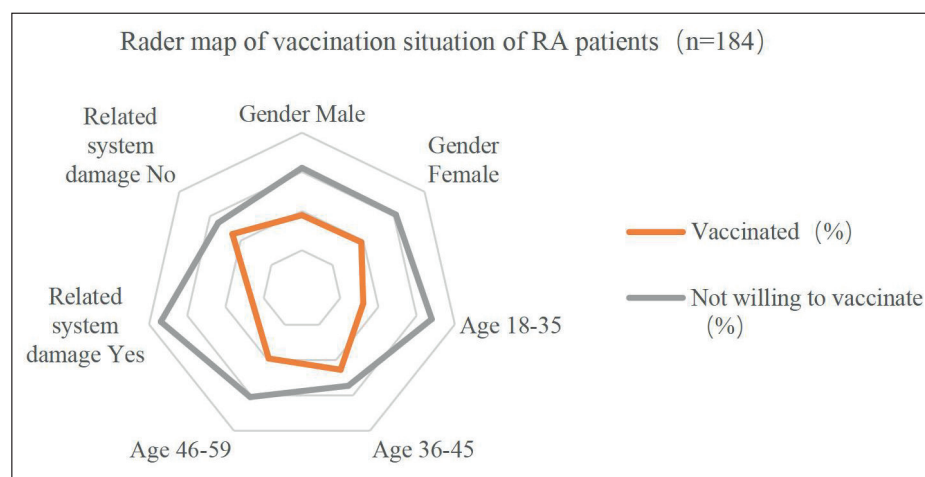


Figure 1. Radar chart of vaccination situation of RA patients (n = 184) in this study. The orange part represents vaccinated, and the gray one represents not vaccinated.

Table 1. Demographic features and disease characteristics toward COVID-19 vaccination in RA patients (n = 184).

Number	Item	Vaccinated or not		p
		Yes (%)	No (%)	
Q1	Gender			0.94
	Male	11 (37.93)	18 (62.07)	
	Female	60 (38.71)	95 (61.29)	
Q2	Age (years)			0.40
	18-35	17 (32.08)	36 (67.92)	
	36-45	20 (45.45)	24 (54.55)	
	46-59	34 (39.08)	53 (60.92)	
Q3	Education level			0.53
	High school and below	46 (35.94)	82 (64.06)	
	University	22 (44.90)	27 (55.10)	
	Master's degree or above	3 (42.86)	4 (57.14)	
Q4	Current marital status			0.30
	Unmarried	7 (28.00)	18 (72.00)	
	Married without child	4 (26.67)	11 (73.33)	
	Married with children	58 (42.65)	78 (57.35)	
	Others	2 (25.00)	6 (75.00)	
Q5	Monthly income(yuan)			0.13
	≤ 5,000	36 (33.96)	70 (66.04)	
	> 5,000	35 (44.87)	43 (55.13)	
Q6	Employment status			> 0.01
	Yes	48 (47.06)	54 (52.94)	
	No	23 (28.05)	59 (71.95)	
Q7	The current payment method for medical expenses			0.12
	Personal expense	18 (30.51)	41 (69.49)	
	Medical insurance	53 (42.40)	72 (57.60)	
Q8	RA duration (years)			0.13
	> 2	31 (34.07)	60 (65.93)	
	2-5	15 (55.56)	12 (44.44)	
	> 5	25 (37.88)	41 (62.12)	
Q9	Related system damage			0.01
	Yes	17 (26.15)	48 (73.85)	
	No	54 (45.38)	65 (54.62)	
Q10	Drugs used within three months			
	Corticosteroid	50 (27.17)	134 (72.83)	0.14
	HCQ	57 (30.98)	127 (69.02)	0.19
	MTX	85 (46.20)	99 (53.80)	0.95
	LEF	51 (27.72)	133 (72.28)	0.82
	bDMARDs	37 (20.11)	147 (79.89)	0.63
Q11	Why didn't you vaccinate?			
	There are contraindications to vaccination.	10 (5.43)	174 (94.57)	0.01
	In the acute stage RA	68 (36.96)	116 (63.04)	<0.01
	Plan for pregnancy	7 (3.80)	177 (96.20)	0.03
	Worried that the disease will worsen due to the discontinuation of Rheumatism drugs during vaccination	53 (28.80)	131 (71.20)	<0.01
	Worried about the side effects of vaccines	61 (33.15)	123 (66.85)	0.08
	There are no cases of COVID-19 in the local area and there is no need to vaccinate.	5 (2.72)	179 (97.28)	0.32
	Vaccination is inconvenient.	4 (2.17)	180 (97.83)	0.58
	Not informed	7 (3.80)	177 (96.20)	0.81
	Vaccine shortage	13 (7.07)	171 (92.93)	0.99
	Currently vaccinated with other vaccines (such as HPV vaccine)	3 (1.63)	181 (98.37)	0.03

Hydroxychloroquine (HCQ), Methotrexate (MTX), Leflunomide (LEF), Biological disease relief anti-rheumatic drugs (bDMARDs), rheumatoid arthritis (RA).

We observed a high proportion (73.85%) of patients ($n = 65$) with a combined systemic impairment who were not willing to be vaccinated ($n = 48$).

Basic Characteristics of Survey Characteristics

Out of the 184 enrolled RA patients, 155 (84.24%) were females and 29 (15.76%) were males. The majority of participants were in the age group of 46-59 years old (47.28%), followed by 18-35 (28.80%) and 36-45 (23.91%) years old. Married individuals accounted for 82.04% of the participants, and the majority of them (67.93%) used medical insurance to pay for their medical expenses. About 35.33% of the participants had combined systemic damage. Regarding vaccination status, as of August 15, 2021, 71 RA patients (38.59%) had been vaccinated against COVID-19, while 113 (61.41%) had not. The no-vaccination rate was lower among unemployed patients (52.94%) than among employed patients (71.95%).

Table I also shows the percentage of the hesitation reasons to get vaccinated among unvaccinated RA patients (Q11). The most common reasons were being in the acute stage of RA (63.04%), planning to get pregnant (96.20%), and concerns about RA worsening due to discontinuation of rheumatism drugs during vaccination (71.20%). Employment status, related systemic damage, plan for pregnancy, and not informing had a statistically significant effect on the decision to not get vaccinated against COVID-19 among RA patients ($p < 0.05$). Detailed information on the socio-demographic and disease characteristics of the study participants and the reasons for VH are presented in Table I.

Univariate Analysis

Furthermore, Chi-square tests were conducted to identify factors that impacted the attitudes and knowledge of RA patients toward COVID-19 vaccination. The results, summarized in Table II, showed that the responses to questions Q14, Q16, and Q18 had a significant impact on COVID-19 vaccination in RA patients ($p < 0.05$).

Table II reveals that 36 participants (65.45%) deemed COVID-19 vaccination to be relatively important, and all 5 patients who deemed it not important remained unvaccinated. Regarding Q14, a total of 7 unvaccinated patients considered the COVID-19 vaccine to be relatively high-risk. As for Q16, 71.68% of unvaccinated RA patients expressed concern that their RA symptoms might worsen following vaccination, and their unvaccinated rate was significantly higher than that of patients who did not share this concern.

As a response to the Q18 “To what extent do you agree that vaccination against COVID-19 is one of the important methods to prevent and control the epidemic?”, RA patients who have been vaccinated have a higher agreement than those who have not been vaccinated ($p < 0.01$). Further details can be found in Table II.

Binary and Multicollinearity Logistics Regression Analysis of the Impact Factor of RA Patients' Cognitive Conditions and Prediction of Intent to Uptake COVID-19 Vaccination

Binary logistic regression analysis indicated that RA patients in the acute stage were less likely to accept COVID-19 vaccination compared to those in the stable phase ($p < 0.001$, OR = -3.165, 95% CI: 0.035 - 0.164).

Respondents who “Worried that the disease will worsen due to the discontinuation of Rheumatism drugs during vaccination” were 3.591 times more likely than individuals who didn't worry ($p < 0.001$, OR = -3.591, 95% CI: 0.005 - 0.157). No significant association was observed between employment status and COVID-19 vaccine acceptance ($p = 0.157$) (Table III). Additionally, participants who believed that the COVID-19 vaccine would affect their ailment were less likely to get vaccinated ($p < 0.001$, OR = -2.365, 95% CI: 0.018 - 0.485), which was shown in Table IV.

In addition, we used a multivariate logistic regression model to evaluate the impact factor of RA patients' cognitive conditions and prediction of intent to uptake COVID-19 vaccination. The non-adjusted and adjusted models are set out in Table V. It was found that the response to Q11 was [“Why didn't you vaccinate? (In the acute stage of RA)” and “Why didn't you vaccinate? (Worried that the disease will worsen due to the discontinuation of Rheumatism drugs during vaccination)”] and to Q16 [“Which aspects are you most concerned about COVID-19 vaccine? (Impact on rheumatism)”] were significant negative independent impact factors for willingness to be vaccinated. See table V for details.

Discussion

The COVID-19 pandemic, triggered by the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 2019, has led to an unparalleled worldwide public health emergency, characterized by substantial morbidity

Table II. Predictors of attitude and hesitancy of COVID-19 vaccine in RA patients (n = 184).

Number	Item	Vaccinated or not		p
		Yes (%)	No (%)	
Q12	Do you think it is important to vaccinate COVID-19 vaccine for RA patients?			0.23
	1	41 (43.16)	54 (56.84)	
	2	11 (37.93)	18 (62.07)	
	3	19 (34.55)	36 (65.45)	
	4	0 (0.00)	5 (100.00)	
	5	0 (0.00)	0 (0.00)	
Q13	Have you known the vaccination guidelines for COVID-19 (the first edition) issued by the China Health and Health Commission in March 2021?			0.26
	Yes	48 (41.74)	67 (58.26)	
	No	23 (33.33)	46 (66.67)	
Q14	To what extent do you agree that vaccination against COVID-19 is one of the important methods to prevent and control the epidemic?			< 0.01
	1	48 (37.80)	79 (62.20)	
	2	12 (29.27)	29 (70.73)	
	3	11 (78.57)	3 (21.43)	
	4	0 (0.00)	2 (100.00)	
	5	0 (0.00)	0 (0.00)	
Q15	Do you think COVID-19 vaccine should be vaccinated for all?			0.93
	Yes	60 (38.46)	96 (61.54)	
	No	11 (39.29)	17 (60.71)	
Q16	Which aspects are you most concerned about COVID-19 vaccine?			
	Security	53 (39.26)	82 (60.74)	0.76
	Curative effect	24 (45.28)	29 (54.72)	0.24
	Impact on rheumatism	32 (28.32)	81 (71.68)	< 0.01
Q17	Do you think COVID-19 vaccine is effective for the SARS-Cov-2?			0.52
	1	16 (34.78)	30 (65.22)	
	2	53 (39.26)	82 (60.74)	
	3	2 (66.67)	1 (33.33)	
Q18	What do you think about the level of risk degree of the COVID-19 vaccine?			
	1	36 (45.00)	44 (55.00)	0.12
	2	19 (38.00)	31 (62.00)	0.92
	3	16 (30.19)	37 (69.81)	0.14
	4	0 (0.00)	7 (100.00)	0.03
	5	1 (100.00)	0 (0.00)	0.21

Table III. Binary logistic analysis of influencing factors of COVID-19 vaccination hesitation in RA patients in China (n = 184).

Number	Item	OR (95% CI)	p
Q6	Employment status	0.157 (0.328 - 4.176)	0.157
Q9	Related system damage	0.99 (0.775 - 9.267)	0.119
Q11	Why didn't you vaccinate?		
	Vaccine shortage	-0.627 (0.086 - 3.316)	0.501
	In the acute stage of RA	-3.165 (0.035 - 0.164)	< 0.01
	Worried about the side effects of vaccines	1.133 (0.7979 - 12.105)	0.103
	Worried that the disease will worsen due to the discontinuation of Rheumatism drugs during vaccination	-3.591 (0.005 - 0.157)	< 0.01

Table IV. Binary logistic analysis of the impact factor of cognitions on COVID-19 vaccination.

Number	Item	OR (95% CI)	<i>p</i>
Q16	Which aspects are you most concerned about COVID-19 vaccine? (Impact on rheumatism)	-2.365 (0.018 - 0.485)	< 0.01
Q18	What do you think about the level of risk degree of the COVID-19 vaccine?	-0.124 (0.052 - 14.966)	0.932

Table V. Multivariate logistic regression analysis of the impact factor of RA patients' cognitive conditions and prediction of intent to uptake COVID-19 vaccination in different models.

Item	Non- adjusted (OR, 95% CI, <i>p</i>)	Adjusted I (OR, 95% CI, <i>p</i>)	Adjusted II (OR, 95% CI, <i>p</i>)
Why didn't you vaccinate? (In the acute stage of RA)	-0.11, (0.05, 0.26), < 0.0001	-0.11, (0.05, 0.25), < 0.0001	-0.11, (0.05, 0.27), < 0.0001
Why didn't you vaccinate? (Worried that the disease will worsen due to the discontinuation of Rheumatism drugs during vaccination)	-0.32, (0.17, 0.60), 0.0004	-0.32, (0.17, 0.60), 0.0004	-0.24, (0.12, 0.49), < 0.0001
Which aspects are you most concerned about COVID-19 vaccine? (Impact on rheumatism)	-0.16, (0.07, 0.38), < 0.0001	-0.16, (0.07, 0.39), < 0.0001	-0.16, (0.07, 0.39), < 0.0001

Non-adjusted model adjusts: None. Adjust I adjust-model for AGE; GENDER. Adjust II adjust-model for Age; Gender; Monthly income (yuan); Current marital status; Related system damage; Rheumatism duration (years).

and mortality²⁴. By August 1st, 2021, the global incidence of COVID-19 infections attributable to SARS-CoV-2 has surpassed 200 million cases²⁵.

During the COVID-19 pandemic, individuals with rheumatoid arthritis (RA) have faced various challenges, including the risk of infection, limited medical resources, medication shortages, and other issues²⁶. RA patients are more susceptible to COVID-19 infection and hospitalization than the general population²⁷.

Vaccination campaigns are the primary approach to reducing the burden of COVID-19. However, there are obstacles such as insufficient information, and vaccine hesitancy (VH) about receiving COVID-19 vaccines may impede the coverage of COVID-19 vaccines²⁸.

The extent of VH, specifically among RA patients, has not been extensively studied. Achieving herd immunity requires a vaccination threshold of 70%²⁹. Globally, there has been an increase in VH in recent years^{30,31}, and vaccination rates for influenza, pneumonia, and other vaccines are generally low among RA patients. Understanding the determinants of VH against vaccines in RA patients is therefore urgently needed³². The objective of this study is to identify vaccination needs, address vaccination-related issues, and ultimately improve vaccination rates.

However, our results showed a lower vaccination rate compared to previous data among healthy individuals who received COVID-19 vaccination³³. Among the 184 RA patients investigated, 113 (61.41%) remained unvaccinated. Employment status and systemic damage were significant barriers to vaccination ($p < 0.05$).

Among RA patients who have not been vaccinated, approximately 75% believe that COVID-19 vaccination may have a negative impact on their RA. VH is significantly influenced by RA patients currently experiencing an acute stage of the disease and those concerned about the progression of their condition due to medication withdrawal. These factors contribute to VH and subsequently impact the COVID-19 vaccination rate of RA patients ($p < 0.001$, OR = -3.165, 95% CI: 0.035 - 0.164; $p < 0.001$, OR = -3.591, 95% CI: 0.005 - 0.157, respectively).

These findings indicate that patients have misconceptions regarding the benefits and risks of the COVID-19 vaccine, which aligns with previous studies investigating the causes of VH in RA patients. These studies^{34,35} have identified various factors contributing to VH, such as perceived high risk of adverse effects, skepticism about vaccine effectiveness, concerns about side effects, and negative attitudes towards vaccines.

A study³⁶ conducted in Italy evaluated VH in patients with rheumatic and musculoskeletal diseases (RMDs) who received the COVID-19 vaccine. It reported a 62% willingness among RA patients to potentially receive the COVID-19 vaccine. Another local multicenter survey³⁷ assessed perceptions of patients with autoimmune diseases (AIDs) regarding COVID-19 vaccination. Although it did not specifically identify VH in RA patients, overall vaccination intentions were lower compared to healthy individuals in China. In India, a survey found that 54% (152/280) of patients with AIDs were willing to receive the COVID-19 vaccine²². An Australian survey³⁸ investigating VH in patients with RMDs and inflammatory arthritis (IA) before and during the pandemic found that 31.8% of IA patients reported VH. Additionally, low vaccination rates for the COVID-19 vaccine may be associated with a failure to seek timely vaccine information from rheumatology professionals.

Based on the results of preliminary clinical trials and real-world applications^{39,40}, the COVID-19 vaccine has been shown to have a positive effect in preventing infection, particularly in reducing the incidence of severe cases and deaths.

However, our findings also revealed that among unvaccinated RA patients, 71.20% were concerned that their condition would worsen after vaccination due to the discontinuation of their rheumatism drugs. This belief was identified as a significant risk factor for VH among RA patients ($p < 0.001$, OR = -0.240, 95% CI: 0.120 - 0.490) based on a logistic regression analysis accounting for multicollinearity.

However, it is important to note that a lack of knowledge about the safety, effectiveness, and disease prevention of vaccines is a known barrier to timely vaccination or refusal of vaccination, thereby putting individuals at risk of preventable diseases. Despite the rapid and complex development of the SARS-CoV-2 epidemic, our research remains of great significance. (1) Improvement of strategies for unknown pandemics: despite the comprehensive lifting of the pandemic, there may still be future threats from other new infectious diseases. By studying VH, we can understand the attitudes and beliefs in defined populations of RA towards new vaccines, providing guidance for improving infectious disease prevention strategies. This is important for enhancing specific populations' trust in vaccine administration, increasing vaccination rates, and reducing the spread of future outbreaks⁴¹. (2) Public health

interventions: Research on VH can also help formulate public health interventions. When facing future outbreaks, policymakers can develop more effective communication strategies and intervention measures based on the results of such studies⁴², in order to quickly establish specific populations' trust in vaccination and improve vaccination rates. (3) Future vaccine development and promotion strategies: understanding the characteristics and related factors of special populations regarding vaccine administration (e.g., patients with rheumatic diseases, cancer patients) also has implications for future vaccine development and promotion strategies¹. These studies can help vaccine development teams better understand the needs, concerns, and anxieties of vulnerable populations, thereby optimizing vaccine design and promotion strategies, and improving the effectiveness and accessibility of vaccination. (4) Global health security: despite the comprehensive lifting of the pandemic, global health security remains an important issue⁴³. Understanding the reasons for VH and the influencing factors can provide lessons and experiences for the formulation of global public health policies and response strategies. These research findings⁴⁴ can serve as references in future health emergencies, strengthening international cooperation and coordination in response to global infectious disease threats. (5) Filling knowledge gaps: the hesitation of special populations towards vaccine administration may not have received sufficient attention in the early stages of the pandemic. Conducting real-time surveys and studies on VH among special populations can help fill these knowledge gaps and enhance our understanding of their vaccination behaviors and attitudes.

When interpreting the findings of this study, it is important to consider several limitations. Firstly, the study sample was recruited from academic clinics and hospitals in China, which may not represent all RA patients, particularly those in remote areas, and therefore, there may be some selection bias. Secondly, the study focused exclusively on the RA population and did not include a comparison of SARS-CoV-2 influenza vaccination rates between RA patients and non-RA patients. The healthy control group was derived from previous literature on normal individuals. Thirdly, the collection of COVID-19 vaccination data relied on self-reported questionnaires, which may have resulted in misclassification bias. Fourthly, online surveys may provide only surface-level information and may not fully

capture a comprehensive understanding of the experiences of RA patients. Fifthly, the evaluation method employed in this study was relatively simple, relying on subjective evaluation through an electronic questionnaire survey, and the sample size was relatively small. Finally, due to the nature of online surveys, some respondents may not have been able to communicate directly with the researchers, potentially leading to biased responses and quality issues.

Conclusions

In conclusion, this work revealed a low COVID-19 vaccination rate among RA patients in China (38.59%), with various factors such as employment status and cognitive attitudes influencing VH. To address this issue and enhance the population's immunity, we recommend the following measures: strengthening vaccine supervision and monitoring to improve response capacity, implementing public education and evidence-based guidance to enhance vaccine literacy, emphasizing the importance of risk communication between specialists and RA patients, and disseminating effective information, and conducting ongoing surveillance of public VH. By implementing these measures, the aim is to increase vaccine uptake among RA patients in China, reduce VH, and ultimately raise overall vaccination rates, thereby enhancing protection against COVID-19 and promoting public health.

Trial Registration

Trial registration number ChiCTR2100049502. Retrospectively registered on 1 August 2021.

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Availability of Data and Materials

The datasets analyzed in this manuscript are not publicly available. Requests to access the datasets should be directed to 15986686048@139.com.

Ethics Approval

This study was approved by Shenzhen Futian Hospital Ethics Committee Shenzhen Futian Hospital for Rheumatic Diseases (No. FS202101001, May 18, 2021, by Shenzhen Futian Hospital Ethics Committee Shenzhen Futian Hospital for Rheumatic Diseases) and was approved by the local administration.

Informed Consent

All participants were informed of the survey's purpose and agreed to keep their personal information strictly confidential.

Conflicts of Interest

The authors declare that they have no competing interests.

Authors' Contributions

Conception and design: H.-Q. Zeng and H.-J. Liu.
Data curation: all authors.
Formal analysis: H.-Q. Zeng and S.-B. Wang.
Investigation: all authors.
Methodology: all authors.
Project administration: H.-Q. Zeng and H.-J. Liu.
Resources: all authors.
Data analysis: H.-Q. Zeng, S.-B. Wang, and Z.-H. Yin.
Supervision: H.-Q. Zeng, Z.-H. Yin, and H.-J. Liu.
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