HUMAN VACCINES & IMMUNOTHERAPEUTICS
2019, VOL. 15, NO. 5, 1100–1105
https://doi.org/10.1080/21645515.2019.1568160

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RESEARCH PAPER

Knowledge, attitude, and practice regarding infection and vaccination in patients with rheumatic diseases in China

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ABSTRACT

Objective Vaccines including pneumococcal and influenza vaccines are recommended in patients with immunosuppressive treatment. However, vaccine coverage remains extremely low. Our study was to investigate vaccination uptake, knowledge, attitude and practice (KAP) towards certain vaccinations among these patients, and to identify the factors influencing willingness to be vaccinated. **Methods** A cross-sectional survey was conducted among patients with rheumatic diseases in a tertiary hospital in China. Baseline assessments were completed by using questionnaires including vaccination uptake and KAP towards certain infections and vaccinations. **Results** 235 patients completed the study. Mean age was 39.69 years old, while 66.4% were females. Only 6.4% of the participants once had taken vaccine in recent five years. One patient had influenza vaccination, and none ever took pneumococcal vaccine. 3.8% had doctor's recommendation on taking influenza, pneumococcal or herpes zoster vaccine. Major reasons given for not being vaccinated included "unnecessary" (8.9%) and "troublesome to take vaccines" (8.5%). Patients would take influenza or pneumococcal vaccines if they had heard of them before, had knowledge of infection, and had belief in vaccine's safety and reliability ($p < 0.05$). **Conclusion** Vaccine coverage among people with rheumatic diseases was low in China. Methods to improve KAP toward infections and vaccinations should be taken.

ARTICLE HISTORY
Received 3 November 2018
Revised 18 December 2018
Accepted 5 January 2019

KEYWORDS
Vaccination; rheumatic diseases; influenza; pneumonia; infection

Introduction

The elderly and other adults with a compromised immune system are considered at high risk of being infected. Pneumococcal disease causes significant morbidity and mortality in both developing and developed countries, causing 1.6 million deaths annually, more than seasonal influenza.[1] The most effective way to prevent infectious diseases in any age group is immunization. Both the Chinese Center for Disease Prevention and Control (China CDC)[2] and the World Health Organization (WHO)[3] recommend prioritizing such adults for annual seasonal influenza vaccination. The United States Advisory Committee on Immunization Practices even updates its current vaccination guidelines annually.[4] Although great efforts have been made in pneumococcal and influenza vaccine distribution since their introduction, significant gap in adult pneumococcal and influenza vaccine coverage persist. In China, vaccine uptake within people at high risk of severe infections remains extremely low. Seasonal influenza vaccine coverage among older adults in China was 8–10.5%.[5] What's more, there was no significant difference in influenza vaccine uptake between those with and without high-risk health conditions.

Two vaccines were offered for adult protection from pneumococcal disease, that is, the 23-valent pneumococcal polysaccharide vaccine (PPV23) and the 13-valent pneumococcal conjugate vaccine (PCV13). A previous study discovered that 19.6% of participants aged over 60 years knew that the vaccination could help prevent pneumonia, but only 2.1% of these participants had taken pneumonia vaccine before in China.[6] Another Chinese study found that few subjects received suggestions from physicians (7.73%), and only 1.23% of the subjects had previously received the 23-PPV vaccination.[7]

Inactivated vaccines that are recommended in patients with autoimmune diseases (ARD). Influenza vaccination and pneumococcal vaccine are routinely recommended to adults using immunosuppressive agents as influenza and pneumonia are among the most common and life-threatening infections. But actual vaccination coverage rate is very low in such patients in China. The reasons may be complicated. Influenza and pneumococcus vaccine are not included in the national Expanded Program on Immunization (EPI), but is available upon request and paid by the individuals. Besides, questions about vaccine safety and efficacy are frequently put forward.[8]

Hepatitis B virus (HBV) infection is very common especially in developing country, including China. HBV vaccination is among compulsory immunization by the Chinese government for the infants at the age of 0, 1, and 6 months since the universal vaccination program in 1992. Although China has made remarkable achievements in the control of HBV infections,[9] the prevalence rate of HBV infection in southern China was reported to be 13.8–16.7%. Vaccination

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is recommended when the risk of infection is increased and protective antibodies are absent.[10]

Human papillomavirus (HPV) is an infection that can be sexually transmitted and result in health consequences including genital warts and cancers. Till now, two vaccines, Gardasil® [Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine] and Cervarix™ [Human Papillomavirus Bivalent (Types 16 and 18) Vaccine] have been approved for the prevention of HPV and HPV-related diseases in China. HPV vaccination should be considered in selected patients with ARD, especially in young women. Patients with ARD should also receive tetanus toxoid vaccination in accordance to recommendations for the general population.[10]

Health-related actions result from individuals' perceived susceptibility to a disease, perceived severity of a disease, perceived benefits of the action to prevent disease, perceived barriers to performing that action and a cue to action.[11] The aims of this study were (1) to investigate the influenza, pneumococcal and other vaccination uptake status among patients with rheumatic diseases; (2) to investigate knowledge and attitude towards certain vaccinations and infections in these patients; (3) to identify the factors influencing immunization uptake among our sample of patients.

Results

General characteristics of the subjects

During the study period, a total of 235 patients were recruited. Mean age of the participants was 39.69 years with a standard deviation of 15.86, and 66.4% (n = 156) of the cohort was female.

First, descriptive statistics and disease characteristics were summarized in Table 1. Seven patients had herpes zoster infection. Four patients had influenza. Five patients had pneumonia. One had dengue fever. And one had herpes genitalis infection in recent five years. 159 (67.7%) of the patients were taking conventional disease-modifying antirheumatic drugs (DMARDs), and nine (3.8%) of the patients were using biological agents. and 143 (60.9%) of patients were taking glucocorticoids.

We found that only fifteen (6.4%) of the participants once had taken vaccine in recent five years. One (0.4%) patient had the influenza vaccination, and none ever took pneumococcal vaccine in recent five years. 220 (93.6%) of the patients had not received any of these vaccines. Rabie vaccine was taken most in this study, followed by HBV, tetanus and HPV vaccine. To be mentioned, none of the nine patients receiving biological agents had taken vaccines in the recent five years.

Table 1. Demographic and disease characteristics of the participants.

Demographic data	Number (%)
Age (years)	39.69 ± 15.86
Gender (males)	79 (33.6)
Disease course (years)	4.48 ± 5.96
Education level (primary school)	38 (16.2)
Education level (university)	78 (33.2)
Language (Mandarin)	97 (41.3)
Language (Cantonese)	76 (32.3)
Language (Dialect)	49 (20.9)
Diagnosis	
▲ SLE	59 (25.1)
▲ Rheumatoid Arthritis	23 (9.8)
▲ Sjogren's Syndrome	20 (8.5)
▲ Systemic sclerosis	15 (6.4)
▲ Other CTDs	13 (5.5)
▲ Vasculitis	10 (4.3)
▲ Spondyloarthritis	19 (8.1)
▲ Gout	40 (17)
Glucocorticoids	143 (60.9%)
cDMARDs	159 (67.7%)
Biological agents	9 (3.8%)

SLE, systemic lupus erythema; cDMARDs, conventional disease-modifying antirheumatic drugs

Knowledge, attitudes and beliefs toward infections and vaccinations

67.7% of the participants had heard of influenza vaccine, while only had heard of herpes zoster vaccine (Table 2). 43.5% of the patients knew they could take vaccine in local community medical service center or hospitals. Only 3.8% of the patients had doctor's recommendation on taking influenza, pneumococcal or herpes zoster vaccine.

Q12 to Q14 tested people's knowledge about function of the vaccines. 58 (24.7%) had correct answers to the three questions. Only 31 patients with immunosuppressive agents treatment or older than 65-year-old knew they should take influenza vaccine because of age and disease.

3.8% of the patients were reported to have tuberculosis, while two more patients were found to have tuberculosis during this study. 28.9% of the patients believed they had the antibodies of HBV. 54.9% of the patients had no idea whether they had the antibodies. 11(4.7%) of the patients were aware of HBV infections and no other people were found to have HBV infections.

The main reasons given for not being vaccinated were as follows:

"unnecessary" (8.9% of the patients), "too expensive" (3.0% of the patients),

"troublesome to take vaccine" (8.5% of the patients) and "no reason" (52.8% of patients).

Factors related to willingness to get influenza and pneumococcal vaccination under doctors' recommendation

There was no statistical difference in age, disease duration, gender between the two groups divided by willingness to get influenza and pneumococcal vaccination under doctors' recommendation (Table 3). Patients were willing to take these two vaccines if they had heard of influenza or pneumococcal vaccine before ($p < 0.05$). Other factors included having correct knowledge of the infection, no worrying of the vaccination fee, having belief in vaccine's safety and reliability, having access to get knowledge about vaccination, knowing the need to get vaccinated, and knowing family members or friends taking influenza or pneumococcal vaccines ($p < 0.05$). However, vaccine uptake in the recent five years, knowing the place for vaccination, and having doctors' recommendation for vaccination before did not differ in the two groups ($p > 0.05$).

Table 2. Questions and answers about disease perception and vaccination.

Number	Question	Yes Or I agreed Number (percentage)	No Or I disagreed Number (percentage)	I didn't know Number (percentage)
Knowledge and attitudes about vaccination				
Q2	Have you ever heard of influenza vaccine?	159 (67.7)	76 (32.3)	-
Q3	Have you ever heard of pneumococcal vaccine?	62 (26.4)	173 (73.6)	-
Q4	Have you ever heard of herpes zoster vaccine?	43 (18.3)	192 (81.7)	-
Q5	Do you know where you can get the vaccine shots mentioned above?	103 (43.8)	132 (56.2)	-
Q12	I won't have flu if I take flu vaccine.	26 (11.1)	117 (49.8)	92 (39.1)
Q13	A person who has not taken flu vaccine will be more likely to get flu than the other people taking flu vaccines.	143 (60.9)	23 (9.8)	69 (29.3)
Q14	I will not easily get pneumonia if taking pneumococcal vaccine.	115 (48.9)	30 (12.8)	90 (38.3)
Q17	Vaccination is safe and reliable.	102 (43.4)	38 (16.2)	95 (40.4)
Q18	It takes huge risks to be vaccinated.	22 (9.4)	116 (49.4)	97 (41.2)
Q19	I have access to get knowledge about vaccination.	75 (31.9)	35 (14.9)	125 (53.2)
Q15	Basic medical insurance would cover influenza and pneumococcal vaccine.	29 (12.3)	22 (9.4)	184 (78.3)
Q16	I am not willing to take influenza and pneumonia vaccination despite fee problem.	36 (15.3)	139 (59.1)	60 (25.5)
Q20	I know I need to take flu vaccine because of my age and disease.	41 (17.4)	33 (14)	161 (68.6)
Q21	I don't know I need to take pneumococcal vaccine because of my age and disease.	79 (33.6)	15 (6.4)	141 (60)
Q22	I know family members or friends taking influenza or pneumococcal vaccines before.	34 (14.5)	47 (20)	154 (65.5)
Q6	Is there any doctor who recommend you to take the vaccine shots mentioned above?	9 (3.8)	221 (94)	5 (2.2)
Q24	I am willing to take influenza or pneumococcal vaccine under doctor's recommendation.	91 (38.7)	44 (18.7)	90 (38.3)
Perception of disease of their own				
Q8	I once had tuberculosis.	9 (3.8)	218 (92.8)	8 (3.4)
Q9	I had antibodies of HBV.	68 (28.9)	27 (11.5)	129 (54.9)
	I had HBV infection.		11 (4.7)	
Knowledge of common infections				
Q10	It won't be serious if I get flu.	44 (18.7)	144 (61.3)	47 (20)
Q11	It could be serious if I have pneumonia.	185 (78.7)	12 (5.1)	38 (16.2)
Vaccination uptake status				
Q1	Vaccination uptake			
	Influenza		1	
	Pneumonia		0	
	Herpes zoster		0	
	HAV		0	
	HBV		3	
	HPV		2	
	Rabies		4	
	Tetanus		2	
	Others		3	
Q23	Reasons given for non-vaccination			
	unnecessary		21 (8.9)	
	too expensive		7 (3.0)	
	troublesome		20 (8.5)	
	No reason		124 (52.8)	

HAV, Hepatitis A virus; HBV, Hepatitis B virus; HPV, Human papillomavirus (HPV)

Discussion

Vaccination could reduce the incidence of getting some severe infections. It is highly recommended in people with high risk factors, including patients with immunosuppressive treatment.[12] In China, vaccines are divided into two categories. As part of the national Expanded Program on Immunization (EPI), Category A vaccines are mandated vaccines provided to children less than 14 years of age at no cost. Category B vaccines, such as influenza vaccine, are not included within EPI; they are optional, and are usually delivered at cost to recipients upon request.[8] The Chinese Preventive Medicine Association (CPMA) updated the guidelines for prevention of pneumococcal disease in 2012, which proposed for the first time that elderly people and the adults at-risk should take the 23-PPV vaccine.[13]

The present survey first confirmed that the coverage rate of certain vaccines, including influenza and pneumococcal vaccine, among Chinese people with rheumatic diseases was extremely low. Only a small proportion (0.4%) of our participants had received influenza vaccination and none (0.0%) had taken pneumococcal vaccine. Interestingly, rabies vaccine enjoys the greatest public awareness, probably due to people's fear of rabies after being bitten by dogs. Vaccination of unregistered dogs against rabies is still neglected in Beijing and other regions of China. Rabies remains a continuous threat to public health in China.[14] Besides, vaccination coverage also differs in countries. In an international COMORA cohort study, only 17.2% of RA patients received pneumococcal vaccination (from 0% in Morocco to 56.5% in France).[15]

The reason why we researchers designed this study was due to the finding in the multi-centered international studies that Chinese patients with rheumatic diseases rarely got vaccinated and seemed to know little about vaccines and even choose not to get vaccinated, compared with the patients in some countries. The questionnaire included several parts, such as his or her vaccination and health condition, knowledge and attitudes of some vaccines, knowledge of some common infections, reasons for unwilling to be vaccinated to help us explore the reason of low vaccination rate. We found that there were complicated reasons why people with rheumatic diseases did not take the vaccines needed. A majority of the participants agreed that pneumonia and influenza could be serious diseases (78.7%, 61.3%, respectively); however, only 38.7% of the participants exhibited a willingness to take pneumonia and influenza vaccines

Table 3. Attitudes, knowledge, and beliefs about influenza and pneumonia vaccinations according to the participants' willingness to take influenza and pneumococcal vaccines under doctors' recommendation.

		Willingness to take influenza and pneumococcal vaccines (Mean ± Standard Deviation, or percentage)		
Variables/Questions	Answers	Yes	No or not sure	P-value
Age	–	37.9 ± 15.65	40.79 ± 15.96	0.20
Disease duration	–	4.49 ± 6.65	4.48 ± 5.49	0.98
Male	–	34.1	31.9	0.74
Have you got vaccination in recent five years?	Yes	9.89	4.17	0.08
	No or not sure	90.1	95.8	
Have you ever heard of influenza vaccine?	Yes	76.9	61.8	0.016
	No or not sure	23.1	38.2	
Have you ever heard of pneumococcal vaccine?	Yes	37.4	19.4	0.002
	No or not sure	62.6	80.6	
Do you know the place for vaccination?	Yes	48.4	41.0	0.267
	No or not sure	51.6	59.0	
There is a doctor who recommends me to take influenza and pneumonia vaccines.	Yes	5.49	2.78	0.29
	No or not sure	94.5	97.2	
It could be serious if I have influenza.	Yes	74.7	52.8	0.001
	No or not sure	25.3	47.2	
It could be serious if I have pneumonia.	Yes	85.7	74.3	0.037
	No or not sure	14.3	25.7	
I am willing to take influenza and pneumonia vaccination with the fee covered by insurance.	Yes	79.1	46.5	□0.001
	No or not sure	20.9	53.5	
Vaccination is safe and reliable.	Yes	60.4	32.6	< 0.001
	No or not sure	39.6	67.4	
I have access to get knowledge about vaccination.	Yes	42.8	33.3	0.004
	No or not sure	57.2	66.7	
I know I need to take influenza vaccine because of my age and disease.	Yes	25.3	12.5	0.012
	No or not sure	74.7	87.5	
I know I need to take pneumococcal vaccine because of my age and disease.	Yes	8.79	5.56	0.337
	No or not sure	91.2	94.4	
I know family members or friends taking influenza or pneumococcal vaccines.	Yes	20.9	10.4	0.026
	No or not sure	79.1	89.6	
A person who has not taken flu vaccine will be more likely to get flu than the other people taking flu vaccines.	Yes	75.8	51.4	□0.001
	No or not sure	24.2	48.6	

under doctors' recommendations. Remaining barriers to vaccination included the patient's perception that they would not benefit from vaccination, wrong beliefs that infections would not be serious problems, no recommendation for vaccination from the doctors and safety issue of the vaccines.

Another public barrier to vaccination may be the cost,[16] especially in China where some vaccines are not covered by insurance. Some patients seemed more willing to take influenza and pneumococcal vaccine if the vaccines were covered by medical insurance. But Yi et al. found that among interviewed unvaccinated older adults on the intervention street, less than 10% listed cost as a major barrier to vaccination.[8] Our study had similar findings that cost was less concerned than other factors in the unvaccinated patients.

Patients with rheumatic diseases are generally treated with immunosuppressive medication. A recent systematic review revealed that pneumococcal and influenza are the two essential vaccines recommended in all immunocompromised patients.[12] In our cohort, 166 (70.6%) of the patients were taking either prednisolone or DMARDs. However, only one of these patients had taken influenza vaccine and none had taken pneumococcal vaccine. It reflected the huge gap between recommendation and implementation in the real world.

To solve the problem of limited vaccine coverage, first of all, healthcare practitioners are responsible for the propagandizing of vaccination. Studies in some countries have demonstrated the positive influence of recommendation on a patient's willingness to get vaccinated.[17-19] 38.7% of our patients were willing to take vaccines with relevant recommendation. A Chinese study also showed that the majority of older adults were reported willingness to get vaccinated if they received a recommendation for vaccination.[8] Strengthening of knowledge about the guidelines related to vaccinations among doctors might effectively elevate the acceptance of vaccination among the people at high risks. Besides, healthcare practitioners could educate people about certain knowledge of infections. Other methods for improving vaccination coverage rates included specific vaccination program objectives, easier access to vaccinations, reduced costs, and increased community demand as instigated by the use of reminders, education and public-awareness campaigns.[20] In addition, the government should not only enhance the supervision of vaccine safety issue, but promote to convey knowledge of vaccines and infections. Scandals related to vaccine shipping have exert tremendously negative effects on the public's beliefs.[21] There is an official website for National immunization program, Chinese CDC, involving knowledge about the vaccination. However, the information are not timely updated and there are only about one hundred thousand visitors till December, 2018.[22]

Our study had some limitations. First, we only included the patients form a single center which was not representative to the population of patients with rheumatic diseases in China. More patients in different rheumatic diseases may lead to robust conclusion and detailed comparison. Second, we used self-reported questionnaires to evaluate the KAP towards vaccination but the reliability of the questionnaire should be examined with caution.

Methods

Participants

The study was carried out from June to December 2017 in a tertiary university hospital in Guangzhou, China. Study participants were patients attending rheumatology inpatient department of the Third Affiliated Hospital of Sun Yat-sen University, which was among top departments of rheumatology in China. This study was conducted in compliance with the Helsinki Declaration to protect human subjects and was

approved by the Third Affiliated Hospital of Sun Yat-sen University ethics committee. All participants were informed of the purpose of survey and verbal consent was obtained before their participation. The response rate in this questionnaire-based study was 97.1%.

Study design

Baseline assessments were completed by trained investigators using identical structured questionnaires including demographic information (age, gender, language frequently used, years of education) and disease related characteristics (diagnosis, age of onset, disease duration, treatment). Self-reported questionnaires were completed by the participants. If the participant had the problem of reading, the investigators would read the questions and answers to help the participant write the answers. The questions were listed in Table 4.

The study instrument was a self-administered questionnaire, which was constructed after a thorough literature review and using the findings of earlier qualitative studies and empirical literature.[6,7,23,24] The draft questionnaire was reviewed by three experts for content validity testing. Expert opinions on the importance and intelligibility of the questionnaire content were considered before the final version was distributed. The questionnaire was mainly divided into 3 parts. The first part included the general characteristics of the participants mentioned above. The second part consisted of questions about self-reported health conditions, recent histories of hepatitis B virus, tuberculosis and other infection. The third part collected information about histories of vaccinations, knowledge and attitude of the participants toward pneumonia, influenza and herpes zoster infection, the efficacy and safety of vaccination, and willingness to get the pneumococcal and influenza vaccination.

The type of vaccine and the time of getting a shot would be recorded if the answer was yes in Question 1. The choices of Question 2 to 6 were yes or no. The choices of Question 7 and 8 were yes, no, or I didn't know. The choices of Question 9 were (a) I had the antibodies, (b) I had no antibodies, (c) I didn't know, (d) I had HBV infection. The choices of Question 10 to Question 22 were (a) I agreed, (b) I disagreed and (c) I didn't know. The choices of Question 23 were (a) I thought it wasn't useful, (b) I thought it was too expensive, (c) I thought it was troublesome, (d) I had no idea, and (e) I would like to get vaccinated. The choices of Question 24 were (a) I would like to, (b) I would rather not to, (c) I still had no idea.

Table 4. Questions related to infection and vaccination in the questionnaire.

NUMBER	QUESTION
Q1	Have you got vaccine shot in recent five years? The types of vaccine included influenza, pneumococcal, herpes zoster, hepatitis A, hepatitis B, Human papillomavirus (HPV), rabies, tetanus and others.
Q2	Have you heard of influenza vaccine?
Q3	Have you heard of pneumococcal vaccine?
Q4	Have you heard of herpes zoster vaccine?
Q5	Do you know where you can get the vaccine shots mentioned above?
Q6	Is there any doctor who recommend you to take the vaccine shots mentioned above?
Q7	Have you ever had pneumonia, influenza or herpes zoster infection in recent five years?
Q8	Did you have tuberculosis before?
Q9	Do you have the antibodies of HBV?
Q10	It won't be serious if I get flu.
Q11	It could be serious if I have pneumonia.
Q12	I won't have flu if I take flu vaccine.
Q13	A person who has not taken flu vaccine will be more likely to get flu than the other people taking flu vaccines.
Q14	I won't easily get pneumonia if I get pneumococcal vaccine.
Q15	Basic medical insurance would cover influenza vaccine and pneumococcal vaccine.
Q16	I am still not willing to get vaccine shots although medical insurance could cover the vaccine fee.
Q17	I believe vaccine is safe and reliable.
Q18	I believe it takes huge risks to be vaccinated.
Q19	I have routes to get known of knowledge about vaccine.
Q20	I know I need to take flu vaccine because of my age and disease.
Q21	I don't know I need to take pneumococcal vaccine because of my age and disease.
Q22	I have family members or friends having taking influenza or pneumococcal vaccine before.
Q23	Why am I unwilling to take influenza or pneumococcal vaccine?
Q24	If now doctors suggest you take influenza or pneumococcal vaccine, are you willing to take the vaccine?

Statistical analyses

Descriptive analysis of the participants was performed, including demographic and disease characteristics. The subjects were divided into 2 groups based on willingness to get influenza and pneumococcal vaccination (yes versus no or not sure) under doctors' recommendation. Independent-sample T-tests and Pearson's x2 tests were used to analyze the differences between these two groups. The analyses were 2-tailed, and P values below 0.05 were considered significant. The Statistical Package for Social Sciences (SPSS) software version 21 were used for all data management.

Conclusion

Vaccinations in patients with rheumatic diseases are of crucial importance due to the increased risk of infections associated with the disease itself and immunosuppressive drugs used. Considering the low vaccination coverage rate in China, more health campaigns to improve the knowledge, attitudes and beliefs toward infections and vaccinations among people with rheumatic diseases are in urgent need.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

Funding

This work was supported a health management platform of spondyloarthritis and hyperuricemia (A2968), and Distinguished Young Scholar Candidates Programme for The Third Affiliated Hospital of Sun Yat-Sen University and Pearl River Nova Program of Guangzhou (Grant No. 201610010005).

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