

Evaluation of pediatric rheumatologists' knowledge, attitudes, and behavior regarding vaccination in pediatric rheumatic diseases

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ABSTRACT

Aim: Developments in diagnostic methods and advances in the treatment of pediatric rheumatic diseases (PRDs) have improved the quality of life in this patient group. However, vaccine-preventable infectious diseases are still outstanding causes of morbidity and mortality in immunocompromised patients more than in healthy population. Pediatric rheumatologists play a critical role in increasing vaccination rates since they have ample opportunity to administer vaccinations. The aim of this study is to determine the knowledge, attitudes, and behaviors of pediatric rheumatologists about vaccination in rheumatic diseases.

Material and Method: Between March 2022-May 2022, an online questionnaire of 20 items was used to evaluate the knowledge, attitudes, and behaviors of pediatric rheumatologists in Turkey with respect to vaccination.

Results: A total of 81 participants answered all survey questions completely. The ages of the study group ranged from 30 to 48 years, at a mean of 37.5 ± 3.8 years. Most of the pediatric rheumatologists (n:76, 93.8%) were working in a tertiary pediatric hospital; 27.2% did not consider themselves primarily responsible for the vaccination of children with PRDs, and 30.9% did not refer their patients to the department that administers the vaccine either before or during immunosuppressive therapy. In addition, it was found that only 14.8% regularly questioned the vaccination history of patients at each outpatient visit. One-third of study group recommended the implementation of non-scheduled vaccines and the most recommended non-scheduled vaccine was seasonal influenza (n:48, 59.3%). The comparative analysis between pediatric rheumatology residents and staff physicians showed no statistically significant difference in the level of knowledge except in the question concerning live vaccines.

Conclusion: This study revealed that there are still serious problems in clinical practice about the vaccination of PRDs patients. For this purpose, pediatric rheumatologists' awareness and knowledge about vaccination should be increased with a special education program.

Keywords: Vaccination, pediatric rheumatic diseases, awareness, knowledge

INTRODUCTION

Developments in PRDs diagnostic methods and advances in treatment, especially the discovery of new generation biological agents, have increased survival and quality of life in this patient group. This results in being more exposed to infectious agents, and consequently these patients are more prone to contracting severe infectious disease (1,2). Vaccination is the most effective, reliable, and affordable way to prevent infectious diseases. The immune system may be suppressed due to drugs used in the treatment of PRDs. In addition, immune dysregulation is common

in the etiology of PRDs. Infections are therefore a major cause of hospitalizations and increased disease activity in these patients (1). Although the protective antibody level provided by a vaccine in this patient group is lower than in healthy people, it is essential to vaccinate children with chronic inflammatory diseases. Serious side effects from the vaccine or active infection due to live-attenuated vaccines may also be seen in these patients whose immune system is affected (3). In addition, vaccination effects may differ from healthy children due to the fact that

PRDs progress with exacerbation attacks and remission. Pediatric rheumatologists are the physicians primarily responsible for regularly following up on these children and thus have a significant window of opportunity to vaccinate patients with PRDs. Since the studies on the efficacy and safety of vaccines in children with PRDs are limited in the literature, pediatric rheumatologists may have concerns about this issue (1, 4).

The aim of this study is to determine the knowledge, attitudes, and behaviors of pediatric rheumatologists about vaccination in rheumatic diseases and concerning patients using immunosuppressive drugs. The data to be obtained in this regard will be important in determining and solving the problems experienced in the vaccination of this patient group.

MATERIAL AND METHOD

The study was carried out with the permission of Ankara City Hospital No 2 Non-interventional Clinical Researches Ethics Committee (Date: 16.03.2022, Decision No: E2-22-1498). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This current study was conducted as a multicenter, cross-sectional, and descriptive questionnaire study. The sample size was calculated on the basis of the number of pediatric rheumatologists working in our country (n=92) with a 95% confidence interval and using the simple random "haphazard sampling" method. The questionnaire, consisting of three different parts and containing a total of 20 questions, was applied to pediatric rheumatologists on an online platform.

The first section comprises 6 questions about demographic characteristics. This section includes questions about age, gender, academic position, number of years worked in the field of pediatric rheumatology, the institution worked at, and the department that administers vaccines in this institution.

The second section of the questionnaire, devoted to the attitudes and behaviors of the participants towards vaccination in patients with PRDs (including COVID-19 vaccines), was evaluated with 7 questions. Finally, in the third section, 7 multiple-choice questions were asked to discern the knowledge level of the participants. This last section pertained to the evaluation of knowledge levels regarding all vaccines administered to pediatric rheumatology patients (both those included in the national immunization schedule as well as non-scheduled vaccines). The accuracy of the data was determined according to the recommendations of the European Alliance of Associations for Rheumatology (EULAR) (5).

All data obtained from the study were evaluated for the entire study group. Afterwards, the participants were categorized into 2 different groups according to their academic positions (residents and staff physicians) and a comparison was made as to whether there was a difference between the groups. Those who had worked in the pediatric rheumatology department for less than 6 months were excluded from the study.

Statistical analysis was performed using IBM SPSS Statistics for Windows Version 21.0 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA). Qualitative data were presented in terms of frequency (n) and percentage (%). Categorical variables are shown in numbers (n), percentages (%) and continuous variables are shown in terms of mean (\pm) standard deviation (SD). The chi-square (χ^2) test was used to compare categorical data. Statistical significance was accepted as $p < 0.05$.

RESULTS

A total of 81 participants completely answered all survey questions. The ages of the study group ranged from 30 to 48 years, at a mean of 37.5 ± 3.8 years. Most of the pediatric rheumatologists (n:76, 93.8%) were working in a tertiary pediatric hospital, and it was found that only 13 (16%) were working in a hospital where vaccinations are not administered. Other demographic data for the study group are given in **Table 1**.

Table 1. Demographic characteristics of the pediatric rheumatologists participating in the survey (n=81), SD, Standard deviation

Characteristic	Total n, (%)
Gender	
Female	65, (80.2)
Male	16, (19.8)
Age, Mean \pm SD	37.5 \pm 3.8
Years of professional experience	
0-3 Years	39, (48.1)
3-6 Years	17, (21.0)
>6 Years	25, (30.9)
In which hospital do you work?	
University Hospital	44, (54.3)
Training and Research Hospital	32, (39.5)
State Hospital	3, (3.7)
Private Hospital	2, (2.5)
What is your academic title?	
Associate professor	17, (21)
Specialist	21, (25.9)
Resident	43, (53.1)
Which department administers the vaccine in your institution?	
Vaccine not administered	13, (16.0)
Pediatric rheumatology department	0, (0)
Pediatric infectious diseases department	4, (4.9)
Social pediatrics department	68, (84.0)

It was determined that 27.2% of the pediatric rheumatologists did not consider themselves primarily responsible for the vaccination of children with PRDs, and 30.9% did not refer their patients to the department that administers vaccines either before or during immunosuppressive therapy. In addition, it was found that only 14.8% regularly questioned the vaccination history of patients at each outpatient visit. The rest inquired into this rarely or only at the first admission. The study group believed that the most important problem regarding vaccination was related to inadequate antibody response to the vaccine. This was followed by a concern for active infection caused by the vaccine strain and an increase in vaccine-related disease activity. The responses of the participants revealing their attitudes and behaviors regarding vaccination are given in **Table 2**.

Table 2. Pediatric rheumatologists attitudes towards vaccination (n=81)

Questions	n, (%)
Which physician is primarily responsible for the vaccination of pediatric rheumatology patients?	
Pediatric rheumatologists	59, (72.8)
Family physicians	32, (39.5)
Social pediatricians	44, (54.3)
Pediatric infectious diseases specialists	18, (22.2)
Do you refer your patients who will be receiving immunosuppressive therapy to the department that administers the vaccine?	
No, I don't.	25, (30.9)
Yes, before the initial treatment	44, (54.3)
Yes, after the initial treatment.	26, (32.1)
Yes, at the end of the treatment	5, (6.2)
What is the biggest problem in pediatric rheumatology practice regarding vaccination?	
Vaccine-related increase in disease activity or severity	17, (21.0)
Serious vaccine-related side effects	9, (11.1)
Active infection caused by the vaccine strain	18, (22.2)
Inadequate antibody and immune response to vaccine	64, (79.0)
No idea	5, (6.2)
Do you question the vaccination history of a patient with a rheumatological disease in daily practice?	
Regularly at every visit	12, (14.8)
Only on the first admission	27, (33.3)
Rarely	36, (44.4)
No, I don't.	6, (7.4)
Do you recommend the COVID-19 vaccine to your rheumatology patients receiving immunosuppressive therapy?	
Yes, I do	81, (100)
No, I don't	0, (0)
If you are recommending the COVID-19 vaccine, is there a vaccine you specifically recommend?	
Coronovac-inactivated vaccine	0, (0)
Biontech-mRNA vaccine	43, (53.1)
I leave it to the patient's choice	38, (46.9)

While almost all of the pediatric rheumatologists thought the implementation of the national vaccination schedule was enough for PRD patients, only one-third recommended the administration of non-scheduled vaccines as well. The most recommended non-scheduled vaccine was seasonal influenza (n:48, 59.3%), and the least recommended was Human Papilloma Virus vaccine

(21.4%). In addition, it was seen that the entire study group recommended the COVID-19 vaccine to their patients. While all of the participants recommended the Biontech-mRNA vaccine, none recommended the Coronovac inactivated vaccine. Data on vaccines recommended by the pediatric rheumatologists are given in **Table 3**.

Table 3. Vaccines recommended by pediatric rheumatologists HPV, human papilloma virus, Men, meningococcal bacteria, HIB, haemophilus influenza type B, BCG, Bacillus Calmette–Guérin

Vaccines	Which vaccine(s) would you recommend for the rheumatology patient? n, (%)
Vaccines in the national schedule	81, (100)
Seasonal influenza	48, (59.3)
HPV	17, (21.4)
Men ACWY	25, (30.9)
Men B	25, (30.9)
HIB	25, (30.9)
Conjugated Pneumococcus	25, (30.9)
Polysaccharide Pneumococcus	22, (27.2)
BCG	34, (42.0)
All scheduled and non-scheduled vaccinations	8, (9.8)

It was found that the entire study group answered the question about inactivated vaccines correctly. However, the rate of those who answered the question about live vaccines correctly was only 60.5%. It was also found that one-third of the participants incorrectly thought that vaccines could increase the severity of rheumatic diseases or cause more serious side effects in patients with PRDs. The lowest correct response rate (18.5%) was found in the question about administering live vaccines to the infant of a pregnant woman using biological agents. The levels of knowledge of the entire group of participants are given in **Table 4**.

In the comparative analysis of the groups, the mean age of the pediatric rheumatology residents (n:43, 53.1%) and staff physicians (n:38, 46.9%), was found to be 37.4±3.7 and 38.5±3.4 respectively. There was no significant difference between the groups in terms of demographic data. The comparison was made to evaluate levels of knowledge based on the correct answers given by both groups to the questions. The number of staff physicians (n:28, 73.7%) who correctly answered the question about administering only live vaccines in line with the national vaccination schedule to children with PRDs was significantly higher than among the residents (n:21, 48.8%) (p. <0.05). The other responses given to the questions that evaluated the level of knowledge were found to show no statistically significant difference between the groups in terms of knowledge levels. Comparative analysis was not performed for the attitude and behavior questions since it was considered that the residents in the group had not as yet attained full competence in daily rheumatology practice.

Questions	Answered correctly n, (%)	Answered incorrectly n, (%)	No idea n, (%)
In all rheumatology patients with stable disease, regardless of treatment, inactivated vaccines can be administered on time, following the national vaccination schedule.	81, (100)	0, (0)	0, (0)
In all rheumatology patients with stable disease, regardless of treatment, live-attenuated vaccines can be administered on time, following the national vaccination schedule.	49, (60.5)	32, (39.5)	0, (0)
In children with active rheumatic disease, the appropriate timing of vaccination should be determined on a case-by-case basis by evaluating the risks and benefits of immunization.	55, (67.9)	26, (32.1)	1, (1.2)
Administered vaccines do not increase the severity of the underlying rheumatological disease.	48, (59.3)	31, (38.3)	2, (2.5)
All administered vaccines do not cause serious side effects in rheumatology patients compared to healthy children.	50, (61.7)	28, (34.6)	3, (3.7)
Treatment of a newly diagnosed rheumatology patient should be initiated after completing the missing vaccines unless the initiation of immunosuppressive therapy is not urgent.	65, (80.2)	11, (13.6)	5, (6.2)
Live vaccines of the infant of a mother using biological agents during pregnancy should be delayed for at least 6 months.	15, (18.5)	16, (19.8)	50, (61.7)

DISCUSSION

Despite increasing evidence supporting vaccine safety and efficacy in children with PRDs, vaccination coverage for these children is still lower than in the healthy population across the world (6, 7). Pediatric rheumatologists play a critical role in increasing vaccination rates since they have ample opportunity to administer vaccinations. To the best of our knowledge, our study is the first study in the literature in our country to evaluate the knowledge, attitudes, and behaviors of pediatric rheumatologists about the vaccinating children with PRDs. Although there is a wide variation among them, pediatric rheumatologists seem to have adequate knowledge regarding vaccination. However, this study revealed that there are still serious problems in this respect in daily clinical practice. The most important problems are that approximately one-third of the pediatric rheumatologists did not regard themselves as responsible for vaccinations and only a very few actually questioned vaccination histories at each visit.

Pediatric romatologists treat a wide spectrum of autoimmune and autoinflammatory diseases. The majority of pediatric rheumatology patients are juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), vasculitides, and autoinflammatory disorders etc. Immunosuppressive medications such as steroid, cyclophosphamide, methotrexate, and biological agents are commonly utilized in treatment. Some children with PRDs have a higher risk of developing infectious diseases compared to healthy children, due to both the immunosuppressive drugs used in treatment and underlying immune dysfunction (1,3). Therefore, effective and safe vaccination is crucial for these patients, but it has been reported that vaccination coverage is inadequate in 1/3 of children with PRDs (6, 7). In a recent cohort that evaluated the vaccination status of 187 children with PRDs, 35% of the children were found to be incompletely vaccinated. In addition, it

was emphasized that the leading reason for vaccination dropout is the advice of the treating rheumatologist (6). In a Canadian study (8) conducted with 200 children with JIA the rate of complete vaccination of patients at the last clinic visit was found to be 61%. In a German study (9) with 715 children with JIA, one-third of the patients were incompletely vaccinated. Moreover, the incomplete vaccination rate was found to be 43.5% in 207 children with PRDs in a Brazil cohort (10). The concerns about vaccines both in parents and patients and an emphasis on contraindications by rheumatologists are seen as the greatest obstacles to vaccination (6, 10). Despite growing evidence, concerns still remain about the safety and efficacy of vaccination. Pediatric rheumatologists should have adequate knowledge about vaccines, especially about their immunogenicity and side effects.

We found in our study that the greatest concern of pediatric rheumatologists about vaccination is inadequate antibody and immune response to the vaccines. The efficacy of vaccines in patients with PRDs is difficult to evaluate. Many factors such as the underlying primary disease, the activity of the disease, the dose and type of immunosuppressive drugs, the type of vaccine administered, and the time of administration, affect the immunogenicity of vaccines (4). Vaccine efficacy studies in the literature have studied protective antibody levels, indicators of immunogenicity, rather than real-life data. These studies have not evaluated all diseases, drugs and vaccines. Nevertheless, the 2011 EULAR recommendations for vaccination in pediatric patients with rheumatic diseases (5) emphasized that the evidence for the efficacy of vaccines is reassuring.

Another concern of rheumatologists and families regarding vaccination is about vaccine safety. Vazhappilly et al. (11), in a survey study evaluating 82 children with PRDs, reported that the most important factor decreasing vaccination rates was the concerns of families

about vaccine safety. It was also found that informing families about vaccine safety and contraindications through rheumatologists increases vaccination rates. Our study shows that half of pediatric rheumatologists have concerns about vaccine safety. In addition, vaccine-related active infection and increased disease activity were found to be the most frequent safety concerns. Many studies have shown that vaccines do not cause serious side effects in children with PRDs compared to healthy children (4), and this is also stated in EULAR recommendations (5). However, it is still debated whether vaccines cause autoimmune disease or increase disease activity. It has been shown in studies performed with measles, mumps, and rubella-MMR vaccine in JIA patients (12) and varicella-zoster virüs-VZV vaccine in juvenile SLE patients (13) that disease activity is not affected by the vaccine in most patients. Data on the use of live attenuated vaccines in patients receiving high-dose immunosuppressive therapy are increasing day by day. The Centers for Disease Control and Prevention (CDC) have defined high-dose immunosuppressive therapy, and it is stated that there is no inconvenience in administering live vaccines in patients receiving low-dose immunosuppressive therapy. However, there is a consensus that live vaccines should be avoided in patients using high-dose immunosuppressive and biologic agents (14,15). In the EULAR guidelines published in 2019 (16), it was emphasized that more research is needed on this issue. In these patients, it seems more appropriate to make a decision on a case-by-case basis, taking into account the risk-benefit ratio. Due to these ongoing discussions in the literature, it is not surprising that pediatric rheumatologists were more concerned about live attenuated vaccines than inactivated vaccines in our study. To address these concerns, it is obvious that well-planned controlled studies are needed to examine rare serious adverse events, particularly in patients using high-dose immunosuppressive drugs, steroids and biologics.

We observed in our study that all of the pediatric rheumatologists considered the implementation of the national vaccination schedule in children with PRDs to be enough. It was not surprising that seasonal influenza was the most recommended vaccine among the special vaccines that are not included in the national vaccination schedule. Seasonal influenza is the most common infection in children with PRDs and poses a risk for lower respiratory tract infection in these patients. The safety and efficacy of influenza and other non-funded vaccines have been proven in these patients (4, 14, 17). The awareness of pediatric rheumatologists about non-funded vaccines will increase the recommendation of these vaccines.

No significant difference was found in our study between resident rheumatologists and staff physicians, except in the matter of the administration of live vaccines. This revealed that the level of knowledge about vaccination is not related to professional experience. In other words, it was observed that the level of knowledge about vaccination did not increase during an individual's rheumatology residency, which is an indication that more education should be provided on vaccinating children with PRDs during the rheumatology education program.

There are some limitations in our study. First of all, the study did not include all pediatric rheumatologists in Turkey because they did not want to participate voluntarily. However, a significant number of participants has been reached. Secondly, the survey questions were designed generically for all PRDs therefore specific diseases and treatment agents were not evaluated. Future researchs may focus on vaccination in specific PRDs like JIA and specific immunomodulatory drugs. However, our study is the first study in our country to evaluate the knowledge, attitudes, and behaviors of pediatric rheumatologists about the vaccinating and contributed to the literature with its significant results.

CONCLUSION

Some patients with PRDs are at a higher risk of infection than healthy children. The most effective way to prevent infections is vaccination, but vaccination coverage for this patient group is not at the desired level due to safety and efficacy concerns. Awareness should be raised and more knowledge should be provided about vaccination during the course of the pediatric rheumatology residency program. Additionally, there is a need for carefully planned randomized controlled studies that will address concerns about vaccination.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara City Hospital No 2 Non-interventional Clinical Researches Ethics Committee (Date: 16.03.2022, Decision No: E2-22-1498).

Informed Consent: Online informed consent was obtained from all participants who participated in this study.

Referee Evaluation Process: Externally peer-reviewed.

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