ASTHMA ALLERGY IMMUNOLOGY
ASTIM ALLERJİ İMMÜNOLOJİ

doi: 10.21911/aai.011
Asthma Allergy Immunol 2022;20:179-183

RESEARCH ARTICLE

Received: 11.04.2022 • Accepted: 21.09.2022
Online Published: 10.10.2022

Pneumococcal Vaccination is a Challenge of Pediatric Allergists

Sinem POLAT TERECE, Hacer Ilbilge ERTOY KARAGOL, Arzu BAKIRTAS

Department of Pediatric Allergy, Gazi University Faculty of Medicine, Ankara, Turkey

Corresponding Author: Sinem Polat Terece ✉ dr_sinempolat@hotmail.com

This study was presented at the 15th Pediatric Allergy and Asthma Congress, S-01, 30 October-2 November 2021, Mugla, Turkey

ABSTRACT

Objective: An increased risk of invasive pneumococcal disease (IPD) has been reported in children with asthma before the introduction of pneumococcal vaccines (PVs). However, the evidence is limited after PV entered the routine immunization schedule. We aimed to investigate whether pediatric allergists recommend additional PV (aPV) to asthmatic children and if so whether there are any asthma-specific risk factors they consider. We also wanted to determine any changes in their recommendations during the COVID-19 pandemic.

Materials and Methods: A questionnaire was e-mailed to all members of the Academy of Pediatric Allergy and Asthma in Turkey. The questionnaire was filled online and consisted of 14 questions.

Results: The questionnaire was e-mailed to 220 members. The response rate was 56.3% and 60.5% of PA recommended aPV. The most frequent asthma specific factors for aPV were severe asthma (70.2%), long term oral corticosteroid use (65.3%) and frequent exacerbations / hospitalizations (62.9%). COVID-19 pandemic increased the rate of questions asked to PA about aPV for asthmatic children compared to previous periods (75.8 vs 33.9%) ($p<0.001$) and %27 of PA changed their recommendations in favor of aPV during pandemic.

Conclusion: Asthmatic children is not infrequent. Severe asthma and related factors seem to be the leading reasons to recommend aPV for asthmatic children. The aPV recommendation by PA is increased during COVID-19 pandemic.

Keywords: Asthma, child, pneumococcal vaccination, COVID-19 pandemic

INTRODUCTION

Streptococcus pneumoniae is still one of the most frequent bacterial agents of invasive diseases in childhood (1). Invasive pneumococcal disease (IPD) is more severe and mortal in patients with underlying chronic diseases than healthy children (2). Asthma is one of the most common chronic diseases of childhood worldwide (3). An increased risk of IPD had been reported in children with asthma before introduction of pneumococcal vaccines (PV). However, the evidence is limited after PV entered the routine immunization schedule (4). We received a lot of calls from parents of asthmatic children for an advise about additional pneumococcal vaccines (aPV) during COVID-19 pandemic. 23-valent pneumococcal polysaccharide vaccine (PPSV23) is recommended after the age of 2 years to asthmatic patients using high-dose oral corticosteroid (OCS) therapy as they are in the high-risk group for IPD (5, 6). We aimed to investigate whether pediatric allergists recommend aPV to asthmatic children and if so whether there are any asthma-specific risk factors they considered. We also wanted to determine any changes in their recommendations during the COVID-19 pandemic.

ORCID Sinem Polat Terece / 0000-0001-7107-5489, Hacer Ilbilge Ertoy Karagol / 0000-0002-8190-062X, Arzu Bakirtas / 0000-0002-7694-8944

MATERIALS and METHODS

We prepared a questionnaire consisting of 14 questions; five of them were related to demographics (Questionnaire). The questionnaire was e-mailed to all members of the Academy of Pediatric Allergy and Asthma in Turkey. It was completed and recorded online. The study was compliant with the Declaration of Helsinki Principles and was approved by the Gazi University Ethics Committee (No: 865).

Statistical Analysis

This is a descriptive study. Continuous variables were presented as mean standard deviation and, median (minimum-maximum); Categorical variables were presented as numbers and percentages. Analyzes were performed with the IBM SPSS Package Program Version 22.0 (IBM Corporation, Armonk, NY, USA). Comparison analyses for categorical variables between independent groups were done by the chi-square test. A p value of <0.05 was accepted as statistically significant.

RESULTS

The questionnaire was e-mailed to 220 members of the Academy of Pediatric Allergy and Asthma in Turkey. The response rate was 56.3%. The responders (n=124) were pediatric allergy specialists (n=91) and fellows (n=33), 96% of whom were working in a tertiary health center. The median age of the physicians was 42 years (min: 30- max: 65) and 74.2% were female. Seventy percent of them had >5 years of experience in allergy and 93.5% recommended additional vaccinations apart from the routine vaccination schedule (Table I). The allergists received more questions about aPV for asthmatic children during the COVID-19 pandemic (75.8%) than before (33.9%) (p<0.001). Risk factors for IPD in asthmatic children perceived by allergists are given in Table II. Risk factors that are non-specific for asthma for aPV recommendation were more frequently chosen by the pediatric allergists compared to asthma-specific risk factors (p<0.001). When we asked pediatric allergists whether asthma patients are in the high-risk group for invasive pneumococcal disease, 47.5% of them answered "yes", 38.7% "no", and 13.7% "I do not know". The most frequent asthma specific factors for aPV were severe asthma (70.2%), long-term oral corticosteroid use (65.3%), and frequent exacerbations/hospitalizations (62.9%). Pediatric allergists recommended 13-valent pneumococcal conjugate vaccine (PCV13), 23-valent pneumococcal polysaccharide vaccine (PPSV23), either one, or both of them in 13.7%, 21%, 8.9% and 16.9%, respectively. During the pandemic, 27% of pediatric allergists changed their recommendations in favor of aPV. The most frequently stated explanations to recommend aPV during the COVID-19 pandemic were the declaration of the Turkish Ministry of Health that asthma is within a risk group of diseases for IPD and in order to reduce secondary lung infections.

Table I. Additional vaccination recommendations by pediatric allergists

	n	%
Any additional vaccination	116	93.5
Influenza	114	91.9
Pneumoccocci	75	60.5
PCV13*	17	13.7
PPSV23	26	21.0
Either of them	11	8.9
Both of them	21	16.9
Meningococci	42	33.9
Rotavirus	35	28.2
Human papilloma virus	30	24.2

* 13-valent pneumococcal conjugate vaccine

Table II. Perspectives of pediatric allergists for invasive pneumococcal disease risk factors among asthmatic children (n=124)

	n	%
Asthma specific		
All asthmatics	28	22.6
Daily ICS use	37	29.8
Biological treatment	74	59.7
Frequent exacerbations/hospitalizations	78	62.9
Long-term OCS use	81	65.3
Severe asthma	87	70.2
Asthma non-specific		
Born before routine PV	83	66.9
Chronic liver disease	93	75.0
Recurrent pneumonia	94	75.8
Chronic kidney disease	95	76.6
Chronic heart disease	95	76.6
Diabetes Mellitus	97	78.2
Chronic lung disease	110	88.7
Immune deficiencies	111	89.5
Anatomic/functional asplenia	112	90.3

Questionnaire

1. Gender
   - ☐ Female
   - ☐ Male
2. Age: .....
3. Academic title
   - ☐ Specialist
   - ☐ Fellow
4. Institution
   - ☐ Public hospital
   - ☐ Training and Research Hospital
   - ☐ Medical Faculty Hospital
   - ☐ Private Hospital
   - ☐ Private Office
5. Job experience
   - ☐ 0-5 years
   - ☐ 5-10 years
   - ☐ 10-15 years
   - ☐ > 15 years
6. Do you recommend additional vaccines to your asthmatic patients outside the routine immunization schedule?
   - ☐ Yes
   - ☐ No
7. Which additional vaccinations do you recommend to your asthmatic patients?
   - ☐ Influenza vaccine
   - ☐ Pneumococcal vaccine
   - ☐ Meningococcal vaccine
   - ☐ Rotavirus vaccine
   - ☐ Human papilloma virus vaccine
   - ☐ Other .....
8. Which pneumococcal vaccine do you recommend as an additional dose to your asthmatic patients?
   - ☐ PCV13
   - ☐ PPSV23
   - ☐ Either of them
   - ☐ Both of them
9. Do you think asthmatic patients are included in the definition of high-risk group for invasive pneumococcal disease?
   - ☐ Yes
   - ☐ No
   - ☐ I do not know
10. Which asthmatic children do you think are at risk of invasive pneumococcal disease?
    - ☐ All asthmatic children
    - ☐ Those born before routine PCV13 administration
    - ☐ Severe asthma
    - ☐ Using daily ICS
    - ☐ Using long term OCS
    - ☐ Using biological agents
    - ☐ Frequent asthma exacerbation or hospitalization requiring OCS use
    - ☐ Chronic heart disease
    - ☐ Chronic lung disease
    - ☐ Chronic liver disease
    - ☐ Chronic renal disease
    - ☐ Diabetes Mellitus
    - ☐ Asplenia
    - ☐ Immunodeficiency
    - ☐ Other .....
11. Have you received questions about additional doses of pneumococcal vaccine from families of asthmatic children before the covid 19 pandemic?
    - ☐ Yes
    - ☐ No
12. Have you received questions about additional l pneumococcal vaccine from families of asthmatic children during covid 19 pandemic?
    - ☐ Yes
    - ☐ No
13. Have you changed your recommendation in favor of additional pneumococcal vaccine during the covid 19 pandemic?
    - ☐ Yes
    - ☐ No
14. Please state the reason about the change in your recommendation of additional pneumococcal vaccine during the covid 19 pandemic period.
    .....

DISCUSSION

The perspectives of allergists about aPV in asthmatic children have not been studied before. We included only pediatric allergists in this study because they see more asthma patients than pediatricians. Most of them were working in a tertiary health center with an allergy experience >5 years that made them reference/consultant physicians for the subject. The most frequently recommended additional vaccines were influenza and PV. It seems that they are more likely to recommend additional vaccines related to their specialty. Considering risk factors nonspecific for asthma to recommend aPV, they frequently chose primary and secondary immune deficiencies related to their specialty.

The most frequent asthma-specific factor to recommend aPV was severe asthma. This approach was supported by two studies (7, 8). Before routine administration of PV, Talbot et al. reported that both children and adults with asthma were at higher risk of IPD than controls and that this risk was greater for severe asthmatics (7). This increased risk of IPD and pneumococcal pneumonia in severe asthmatic children continued after routine administration of PV compared to children with no known risk (8).

Allergists declared prolonged OCS use (long term or asthma exacerbation/hospitalization) as the second asthma-specific factor to recommend aPV. In reality, this is a well-known, widely accepted risk factor for IPD (5, 6). It may be difficult to discriminate whether severe asthma or prolonged OCS use in asthma has a greater effect on the development of IPD. Prolonged OCS use may not be the main risk factor for pneumococcal pneumonia in children (8). In the Pelton et al. study, the pneumococcal pneumonia risk was increased 2-3 fold in children 5-17 years old with no asthma diagnosis with ≥30 days of oral steroid use. However, the risk was shown to increase >10 fold in children with severe asthma compared to children with prolonged OCS use (8).

Another risk factor to recommend aPV was treatment with biologicals. Although biologicals may be thought to increase the IPD risk due to severe asthma, the opposite is also possible by providing disease control. Unfortunately, there is no evidence about the effect of biologicals on IPD, yet.

A considerable percent of allergists thought that even daily inhaled corticosteroid (ICS) use increases the risk for IPD. In fact, daily long-term ICS use was associated with increased risk of pneumonia requiring hospitalization compared to non-users and the risk was greatest at higher ICS doses and remained significant even with lower doses (9). On the other hand, 22% of the allergists recommend aPV to all asthmatic children. This approach may also be true according to the recent meta-analysis that revealed children with asthma who received pneumococcal conjugate vaccine (PCV) as part of their regular immunization schedules still have 90% higher odds of IPD than children without asthma (4). Therefore they suggest that children with asthma >2 years of age should receive PPSV23 after their regular PCV vaccination schedule irrespective of the use of high-dose oral steroids

These findings suggest that even pediatric allergists are confused about whether asthma is an indication for aPV and if so which asthmatic children should be vaccinated. Besides, they are not determined about the type of PV, either. We think that increased queries about aPV from families during the COVID-19 pandemic might have further increased this confusion such that more than a quarter of pediatric allergists changed their recommendations in favor of aPV during this period. We believe that this confusion is probably related to the limited number of studies at the beginning of the COVID-19 pandemic (4, 8). As data accumulated during the pandemic, it was found that asthma and its treatment are not risk factors for morbidity and mortality associated with a COVID-19 infection (10, 11). In addition, a prospective cohort study in young children showed that the COVID-19 pandemic was associated with reduced rates of IPD with no change in nasopharyngeal pneumococcal carriage (12). The pneumococcal serotypes related to IPD did not change during the pandemic, either (13). It is hypothesized that reduced dynamics of pneumococcus-associated disease rates were temporally associated with the reduced dynamics of respiratory viruses (12). In addition, no IPD/COVID-19 coinfections were reported in children in contrast to adult patients (13).

The questionnaire-based methodology is the major limitation of the study and may not reflect the real practice of allergists regarding aPV. However, the study also has strengths such as including only pediatric allergists who are at the top position to care for asthmatic children and evaluating the effect of the COVID-19 pandemic to the study subject.

In conclusion, even pediatric allergists are confused about whether to use aPV in asthmatic children, whether to vaccinate all or a subgroup of asthmatics, and which PV to choose: conjugate or polysaccharide. Certainly, the consensus of physicians about vaccination is important not only for the primary prevention of diseases but also as an action against vaccine hesitancy (14). Therefore, well-designed prospective follow-up studies are needed in order to overcome the confusion of allergists and to provide the optimum prophylaxis for IPD in children with asthma.

Acknowledgements

We thank the Academy of Pediatric Allergy and Asthma for supporting the study by e-mailing the questionnaire to its members.

Conflict of Interest

We certify that we have no actual or potential conflicts of interest in relation to this article.

Authorship Contributions

Concept: **Sinem Polat Terece, Arzu Bakirtas,** Design: **Arzu Bakirtas,** Data collection or processing: **Sinem Polat Terece,** Analysis or Interpretation: **Sinem Polat Terece, Hacer Ilbilge Ertoy Karagol, Arzu Bakirtas,** Literature search: **Sinem Polat Terece, Arzu Bakirtas,** Writing: **Sinem Polat Terece, Hacer Ilbilge Ertoy Karagol, Arzu Bakirtas,** Approval: **Sinem Polat Terece, Hacer Ilbilge Ertoy Karagol, Arzu Bakirtas.**

REFERENCES

1. Tan TQ. Pediatric invasive pneumococcal disease in the United States in the era of pneumococcal conjugate vaccines. Clin Microbiol Rev 2012;25:409-19.
2. Kaplan SL, Mason EO Jr, Wald E, Tan TQ, Schutze GE, Bradley JS, et al. Six year multicenter surveillance of invasive pneumococcal infections in children. Pediatr Infect Dis J 2002;21:141-7.
3. Beasley R, Semprini A, Mitchell EA. Risk factors for asthma: Is prevention possible? Lancet 2015;386:1075-85.
4. Castro-Rodriguez JA, Abarca K, Forno E. Asthma and the risk of invasive pneumococcal disease: A meta-analysis. Pediatrics 2020;145:e20191200.
5. Nuorti JP, Whitney CG; Centers for Disease Control and Prevention (CDC). Prevention of pneumococcal disease among infants and children - use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine - recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2010;59(RR-11):1-18.
6. American Academy of Pediatrics Committee on Infectious Diseases. Recommendations for the prevention of Streptococcus pneumoniae infections in infants and children: Use of 13-valent pneumococcal conjugate vaccine (PCV13) and pneumococcal polysaccharide vaccine (PPSV23). Pediatrics 2010;126(1):186-90.
7. Talbot TR, Hartert TV, Mitchel E, Halasa NB, Arbogast PG, Poehling KA, et al. Asthma as a risk factor for invasive pneumococcal disease. N Engl J Med 2005;352:2082-90.
8. Pelton SI, Weycker D, Farkouh RA, Strutton DR, Shea KM, Edelsberg J. Risk of pneumococcal disease in children with chronic medical conditions in the era of pneumococcal conjugate vaccine. Clin Infect Dis 2014;59:615-23.
9. Qian CJ, Coulombe J, Suissa S, Ernst P. Pneumonia risk in asthma patients using inhaled corticosteroids: A quasi-cohort study. Br J Clin Pharmacol 2017;83:2077-86.
10. Papadopoulos NG, Custovic A, Deschildre A, Mathioudakis AG, Phipatanakul W, Wong G, et al. Impact of COVID-19 on pediatric asthma: Practice adjustments and disease burden. J Allergy Clin Immunol Pract 2020;8:2592-99.
11. Papadopoulos NG, Mathioudakis AG, Custovic A, Deschildre A, Phipatanakul W, Wong G, et al. Childhood asthma outcomes during the COVID-19 pandemic: Findings from the PeARL multi-national cohort. Allergy 2021;76:1765-75.
12. Danino D, Ben-Shimol S, Van Der Beek BA, Givon-Lavi N, Avni YS, Greenberg D, et al. Decline in pneumococcal disease in young children during the COVID-19 pandemic in Israel associated with suppression of seasonal respiratory viruses, despite persistent pneumococcal carriage: A prospective cohort study. Clin Infect Dis 2022;75(1):e1154-64.
13. Amin-Chowdhury Z, Aiano F, Mensah A, Sheppard CL, Litt D, Fry NK, et al. Impact of the coronavirus disease 2019 (COVID-19) pandemic on invasive pneumococcal disease and risk of pneumococcal coinfection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Prospective national cohort study, England. Clin Infect Dis 2021;72:65-75.
14. Turner PJ, Larson H, Dubé È, Fisher A. Vaccine hesitancy: Drivers and how the allergy community can help. J Allergy Clin Immunol Pract 2021;9:3568-74.