

Schedule of pneumococcal conjugated vaccination and incidence of asthmatic exacerbation in children

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Abstract

Background: Chronic asthma is a complex condition. An abrupt rise in eosinophil counts, deterioration of asthma symptoms, increased reliance on bronchodilators with or without oral/IV corticosteroids, and a higher frequency of emergency room visits with hospitalisations or antibiotic use have been identified as indicators of the effectiveness of the pneumococcal conjugate vaccine in preventing illness.

Aim: The objective of this study was to assess the clinical importance of scheduling the pneumococcal conjugate vaccine in reducing the occurrences of asthma exacerbations and their subsequent complications in children, as previously described.

Methods: A study at Queen Rania Abdullah for Children Hospital in Amman, Jordan, examined 200 children aged 3-14 with chronic asthma who were hospitalized from 2022 to 2023 due to wheezing. The children were divided into four groups based on their experience with the flu vaccine and PCV13. The study used a detailed questionnaire to gather information about the children's background, health history, vaccination history, and vaccination history. The results were analyzed using chi-square testing and a 95% confidence interval.

Results: A paediatric clinic in Jordan had 200 asthmatic kids, with 40.5% having not received the flu or PCV13 shot. The remaining 43.5% had received the flu shot but forgot to get the PCV13. About 11% of the kids in Group II were asthmatic and received both the flu shot and PCV 13. The study found a positive correlation between Groups I-IV for men but not for women. Age groups had similar distribution rates, with 21.0% for ages 3 to 6, 34.0% for ages 6 to 9, 37.5% for ages 9 to 12, and 7.5% for ages 12 to 15. There was a strong link between the rates of wheezing episodes in Groups I through IV compared to rates of occasional versus frequent episodes in the past seasonal year.

Keywords: Pneumococcal conjugate vaccination; Children with asthma; Exacerbation of asthma; Estimation of risk; Clinical impacts of the vaccine

1. Introduction

An estimated 100,000 episodes and 100 deaths per million children under the age of five are attributed to lower respiratory infections (LRIs), a condition that is estimated to have lower rates in paediatric asthma patients older than five. For instance, 52.3% of LRI deaths are caused by pneumococcal pneumonia, whereas influenza accounts for 1.28% of cases. A major global health concern, pneumococcal infections result in approximately 294,000 deaths annually among children under five, with China accounting for roughly 12% of these cases. Vaccination against pneumococcal

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and influenza, however, can both lessen the burden of disease. Thirteen common pneumococcal serotypes are protected against by the PCV13 vaccine. Owing to immunogenicity similar to that of PCV7, PCV13 was approved for use in China in 2016 and formally introduced in various provinces in 2017. Currently, infants and children aged 6 weeks to 5 years are administered PCV13 after a 3-dose primary series that includes a booster dose. Approximately \$100 per dose could be a barrier to widespread adoption, particularly in developing nations.¹⁻³

In Singapore, the Ministry of Health advises, for example, that children between the ages of six months and five receive an annual dose of the inactivated influenza vaccine and that children between the ages of three and twelve months receive three doses of the 13-valent pneumococcal conjugate vaccine (PCV-13). Vaccinations against measles, mumps, rubella, diphtheria, tetanus, pertussis, hepatitis B, polio, Haemophilus influenza type B, and tuberculosis are also advised. But according to various institutional internal protocols and contingent on agreement between the physician and the parents of the affected asthmatic children, the Ministry of Health in Jordan recommends all of the previously mentioned vaccines, with the exception of the two primary vaccines of interest in this study, the flu vaccine and PCV 13.⁴⁻⁶

In reality, despite national guidelines and the growth of funding programmes, influenza and PCV uptake are still below par. Compared to other vaccinations like measles, polio, and diphtheria, PCV coverage increased from 17% in 2009 to 82% in 2019, according to national estimates in the United States. However, this is still lower. The disease and mortality associated with *S. pneumoniae* are successfully reduced by pneumococcal conjugate vaccines (PCVs). Pneumococcal infections are a major priority for vaccination programmes to prevent, according to the World Health Organisation. In 144 countries, PCVs are part of national immunisation programmes. According to a prior study, 15% of preschool-aged children received the influenza vaccine in the previous year. Numerous sociodemographic factors are among the complex reasons for the low vaccination rate. In contrast to parents of PCV-vaccinated children, parents of PCV-unvaccinated children were less likely to be aware of pneumococcal disease or the PCV vaccination, and they were also less willing to pay for the shot out of pocket, according to a survey conducted in Singapore among 162 parents.⁷⁻⁹

Due to the recent introduction of PCV13 and the paucity of comprehensive national surveillance data on pneumococcal infections, evaluating the specific effects of the virus is challenging. To strengthen preventive measures against pneumococcal infections, policymakers require a targeted assessment of PCV's effects. The effects of PCV13 on different forms of pneumonia and invasive pneumococcal disease are the main focus of current observational studies.¹⁰⁻¹¹ Thus, the main goal of this research was to find out if there was a significant difference in the rates of wheezing in children with stable asthma who received the annual flu shot, either alone or in combination, or if receiving one shot increased the frequency of occasional wheezing episodes to four or more. Another secondary goal of this research was to compare the gender and age categories across the four predefined PCV13- and flu vaccine-based groups between the tested variables.

2. Methods

At the Queen Rania Abdullah for Children Hospital in Amman, Jordan, the study was done after the fact. It was approved by the Institutional Committee for Ethics in Research under the registration number 57_2/2024. In our paediatric clinic for children with chronic asthma, 200 kids between the ages of 3 and 14 were hospitalised from the start of 2022 to the end of 2023 because they kept wheezing. If someone has had at least four recorded wheezing episodes, they were considered to have frequent wheezing. If they had less than four episodes, they were considered to have occasional wheezing. According to CDC guidelines, the study had criteria like a minimum of 12 months having passed since the last annual flu shot and an asthma attack.

No matter how bad the asthma attack was, signs included needing to go to the hospital or take systemic corticosteroids with or without antibiotics, or needing more rescue medication after the attack, and the need for more rescue medication after the attack. This study didn't include any kids whose asthma had been uncontrolled or partially controlled for the past 12 months, even if they had wheezing episodes. The parents of the asthmatic and vaccinated children who were part of our study did not have to give informed consent because it was an observational and retrospective study. To get complete information, it is important to first find out the age and gender of the children being tested, as well as how many wheezing attacks they have had in the past. According to the National Vaccination Schedule (NVS), a child was fully vaccinated if they had gotten all of their shots.

All the asthmatic kids who were tested will be put into four groups based on their experience with the flu vaccine and PCV13. Group I will have never had either the flu vaccine or PCV13, Group II will have had the flu vaccine but not PCV13, Group III will have had both the flu vaccine and PCV1 and Group IV will have never had either the flu vaccine or PCV13. As part of the statistical analysis, the model's fit was checked, the Pearson chi-square statistic was calculated, and the

Chi Square Test was carried out. We used chi-square testing to find the Pearson correlation @ correlations for each variable that we wanted to compare. The results were given as correlation values with standard errors.

A detailed questionnaire was given that asked about the person's background and health, including their parents' education level, family income, number of siblings, history of vaccinations, wheezing episodes in the past, place of residence, length of breastfeeding, use of antibiotics as a baby, recent antibiotic prescriptions, and how often they inhaled corticosteroids. As long as kids got their shots according to the National Vaccination Schedule (NVS), their vaccination record was full. For something to be significant, the P-value had to be less than 0.05 or the odds ratio had to have a 95% confidence interval (CI) that didn't include 1.00.

3. Results

A paediatric clinic in Jordan had 200 asthmatic kids. Of those, 40.5% (81 kids) had not gotten either the flu shot or the PCV13 shot, so they were put in Group I. The other 43.5% (87 kids) had gotten the flu shot the year before but forgot to get the PCV13 as planned. About 11% of the kids in Group II were asthmatic, and they got both the flu shot and PCV 13. Finally, only about 5% (10 asthmatic kids) had only experienced PCV13 and had never had a flu shot. Comparing the number of male and female patients in the four groups (Groups I–IV), 36% were female (72 out of 200) and 64% were male (128 out of 200).

In Groups I–IV, there were no big differences in the rates of distribution between men and women. However, there were more males in the paediatric cohort than females in any of the other groups [53 (65.4%) vs. 28 (34.6%), 50 (57.5%) vs. 37 (42.5%), 19 (86.4%) vs. 3 (13.6%), and 6 (60.0%) vs. 4 (40.0%): The Pearson correlation test showed that there was a positive correlation between Groups I–IV for men but not for women. It had a chi-square value of $X^2(3) = 6.527$ and a p-value of 0.089. The correlation coefficient was $+0.037 \pm 0.069$.

When we tested the age groups that were 3 years apart, we found that Groups I and II had similar distribution rates. Over all, the rates were 21.0% for ages 3 to 6, 34.0% for ages 6 to 9, 37.5% for ages 9 to 12, and 7.5% for ages 12 to 15. The Pearson correlation coefficient (R) and its standard error values showed a negative relationship that was not statistically significant (-0.012 ± 0.078 , $X^2(9) = 8.756$, 0.460).

There was a strong link between the rates of wheezing episodes in Groups I through IV compared to rates of occasional episodes versus frequent episodes in the past seasonal year. With a value of -0.256 ± 0.051 , the Pearson correlation coefficient was slightly negative and significant ($X^2(3) = 20.973$, p-value=0.000). There were no frequent wheezing episodes in the experienced PCV13 and naïve flu vaccine group (Group III) or in the experienced PCV13 with naïve flu vaccine group. However, there were 22 (100.0%) and 10 (100.0%) occasional wheezing episodes. In the naïve flu vaccine and PCV13 group (Group I), the rates of frequent wheezing versus occasional wheezing were 34 (42.0%) vs. 47 (58.0%), respectively. In the experienced flu vaccine but naïve PCV13 cohort (Group II), the rates were 37 (42.5%) vs. 50 (57.5%).

4. Discussion

The purpose of this study was to identify sociodemographic variables related to the vaccination uptake of pneumococcal and influenza among preschool-aged asthmatic children, beginning at age three, as well as the school-age asthmatic children whose asthmatic status is classified as controlled stable on prescribed medication in Jordan. However, a number of earlier studies that examined the multifaceted potential confounders of demographic, educational, geographic, genetic, environmental, residential, parenteral, pathological, psychological, and historical factors in addition to the annual flu shot and the three scheduled pneumococcal vaccinations have found evidence against the tendency for the completeness of standard immunisation schedules.¹²⁻¹³

According to the previously mentioned studies, children who had previously been hospitalised for cough were 1.77 times more likely to receive the annual influenza vaccination than children who had never experienced a hospitalisation for cough. The yearly flu shot was also positively correlated with household income, housing type, smokers in the home, parental educational attainment, child age, and asthma. However, even though the majority of the findings were statistically insignificant, some studies unexpectedly showed a negative correlation between the child's age, the parental education level, and the uptake of the influenza vaccine.¹⁴⁻¹⁵

Table 1 Comparatively studied variables across Cohort I-IV

	Group I	Group II	Group III	Group IV	Total	R±SEV	X2 (df) Sig
	Naïve both Flu Vac & PCV 13	Experienced Flu vac but Naive PCV13	Experienced both Flu Vac & PCV13	Naive Flu vac but Experienced PCV13	200		
	(81, 40.5%)	(87, 43.5%)	(22, 11%)	(10, 5%)			
Gender							
Female	28 (34.6%)	37 (42.5%)	3 (13.6%)	4 (40.0%)	72 (36.0%)	+0.037±0.069	(3) 6.527 0.089
Male	53 (65.4%)	50 (57.5%)	19 (86.4%)	6 (60.0%)	128 (64.0%)		
Age (years)							
3-6	15 (18.5%)	17 (19.5%)	6 (27.3%)	4 (40.0%)	42 (21.0%)	-0.012±0.078	(9) 8.756 0.460
6-9	30 (37.0%)	31 (35.6%)	5 (22.7%)	2 (20.0%)	68 (34.0%)		
9-12	32 (39.5%)	33 (37.9%)	7 (31.8%)	3 (30.0%)	75 (37.5%)		
12-15	4 (4.9%)	6 (6.9%)	4 (18.2%)	1 (10.0%)	15 (7.5%)		
Wheezing episodes							
Occasional	47 (58.0%)	50 (57.5%)	22 (100.0%)	10 (100.0%)	129 (64.5%)	-0.256±0.051	(3) 20.973 0.000
Frequent	34 (42.0%)	37 (42.5%)	0 (0.0%)	0 (0.0%)	71 (35.5%)		
Flu Vac							
Naive	60 (74.1%)	0 (0.0%)	0 (0.0%)	10 (100.0%)	70 (35.0%)	+0.336±0.092	(3) 131.624 0.000
Experienced	21 (25.9%)	87(100.0%)	22 (100.0%)	0 (0.0%)	130 (65.0%)		
PCV 13							
Naive	75 (92.6%)	87 (100.0%)	0 (0.0%)	0 (0.0%)	162 (81.0%)	+0.672±0.058	(3) 163.902 0.000
Experienced	6 (7.4%)	0 (0.0%)	22 (100.0%)	10 (100.0%)	38 (19.0%)		
Data results of the comparative variables between the 2 tested cohorts were statistically analyzed by Chi-Square Test (at p-value< 0.05) and expressed as Numbers (Percentage). The strength of associations was also described as odd ratios (OR). The Pearson chi-square statistic (χ^2) involves the squared difference between the observed and the expected frequencies. The Goodness of Fit (G-Test of independence) uses the log of the ratio of two likelihoods and tests the goodness of fit of observed frequencies to their expected. Both the interval by interval (Pearson, r) and the ordinal by ordinal (Spearman, ρ) correlations were expressed as value± standard error of value.							

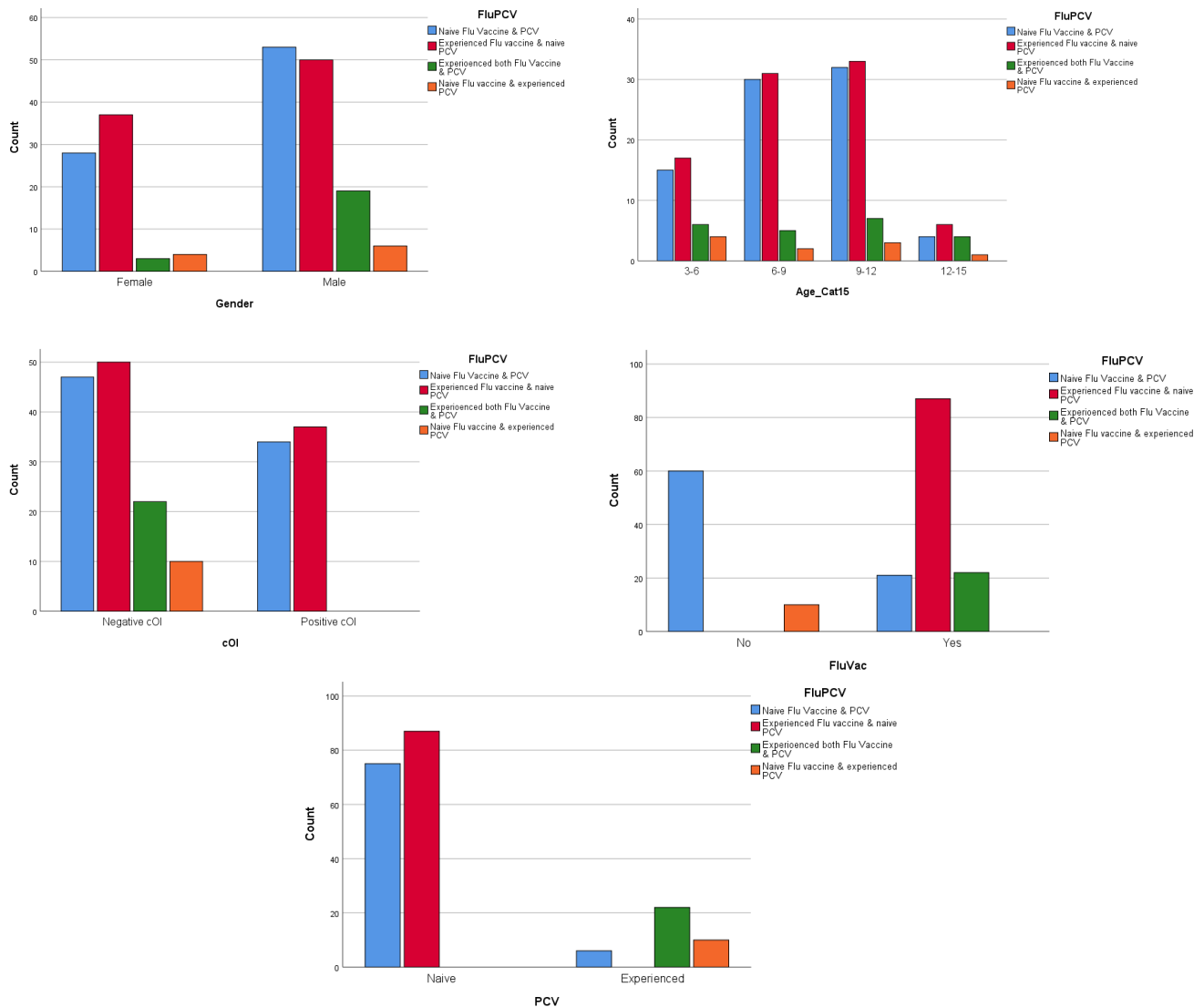


Figure 1 Bar illustration for the comparative variables

Indeed, in the multivariable analysis, the following variables—particularly for the 13-valent polysaccharides (PCV 13) as opposed to the 7-valent polysaccharides (PCV 7)—were significantly associated with influenza vaccination with or without receiving the pneumococcal conjugated vaccination as scheduled: residential place (Urban >Rural), type of housing (Landed property>Public housing), and previous hospitalisation (positive hospitalisation history>negative history). Additional variables that were statistically significant in the univariable analysis included household smoking statuses (Lower>Higher), overall household income, and educational attainment (Higher > Lower). where smokers in the home were negatively associated with timely annual flu vaccination and PCV scheduled uptake, while the highest parental education level and monthly household income were positively associated. ¹⁶⁻¹⁸

While some studies found that households with at least one college-educated parent were 2.12 times more likely than households with no college-educated parent to vaccinate their children against PCV, the relationship was not statistically significant. Other studies found that positive household smoking was still statistically significant when combined with PCV but not with flu vaccination, even after multivariable analysis. This finding could be explained by the fact that pneumococcal vaccination has a higher potential for conjugation due to its polysaccharide valent nature, especially when given on a scheduled schedule, compared to the annual flu vaccination. ¹⁹⁻²¹

Our study, which demonstrated a strong correlation between the rates of wheezing episodes in the four flu vaccines under investigation and PCV13-based classification of Group I-IV as frequent episodes versus occasional episodes, made these phenomena abundantly evident. The Pearson correlation coefficient ($X^2(3) = 20.973, p\text{-value} = 0.000$) showed a slightly negative and significant value of -0.256 ± 0.051 . Neither the experienced PCV13 with naïve flu vaccine

group (Group III) nor the experienced PCV13 with naïve flu vaccine group experienced frequent wheezing episodes. Nonetheless, 10 (100.0%) and 22 (100.0%) individuals occasionally experienced wheezing episodes. The rates of frequent versus occasional wheezing were 34 (42.0%) and 47 (58.0%) in the naïve flu vaccine and PCV13 group (Group I), respectively. Group II, the PCV13 cohort with prior flu vaccination experience, had rates of 37 (42.5%) compared to 50 (57.5%).

Owing to certain limitations, including a small sample size, a single-center retrospective observation, and the failure to account for potentially confounding sociodemographic variables, we were only able to find a significant association between receiving the pneumococcal conjugated vaccination and the prevention of wheezing episodes in our tested attended children aged 3 to 15 years, regardless of whether they received the annual flu vaccinations. This prevented the wheezing from worsening into an advanced, frequent state where there were four or more clinically significant attacks within the previous six months, which required the use of an asthmatic inhaler, the administration of antibiotics, paediatric emergency visits, and the administration of corticosteroidal intravenous or nebulize. Nonetheless, it is anticipated that the influenza vaccine, when administered on a timely and regular basis each year, along with the pneumococcal vaccination given beforehand and the comprehensiveness of the recommended immunisation regimen, will provide the greatest possible benefit to our children, particularly those who suffer from long-term conditions like asthma.²²⁻²³

5. Conclusion

In this study, we observed a negative correlation between receiving the annual flu vaccination on time, along with or without a prearranged pneumococcal vaccination as conjugated polysaccharides 13 valent, and experiencing frequent wheezing episodes instead of being stable or stabilized at an occasional state in attended children with affected asthma. Furthermore, as this observational single centre retrospective study demonstrated, the annual flu vaccination was not primarily responsible for the statistically significant negative correlation, but rather the previously administered PCV13. More thorough research and guidelines seem to support the idea that receiving both the flu shot and the pneumococcal conjugated vaccine will largely improve children's quality of life in general, especially for those whose children have asthma. Pediatricians and other healthcare professionals should strongly advocate for this issue.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest in this manuscript.

Statement of ethical approval

There is no animal/human subject involvement in this manuscript.

Statement of informed consent

Owing to the retrospective design of this study, the informed consent form was waived.

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