

Prevnar-20 And Acute Exacerbation Of Reactive Airway Disease: A Case-Control Study.

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Abstract

Background: Acute exacerbation of RAD in the pediatric population is distressing not only to the patient and their families, but also to the healthcare system. By preventing the number of episodes of acute exacerbation of RAD, we will be making a difference for patients and their families.

Objective: We aimed to assess the effectiveness of Prevnar-20 vaccine against hospitalization for acute exacerbation of RAD among children younger than 4 years of age.

Methods: This is a retrospective, unmatched case-control study done at UTMB, based on chart reviews. Cases consisted of patients who received Prevnar-20, and the control group included patients who received PCV-13. The primary end point was the number of episodes of RAD exacerbation after receiving prevnar-20. The secondary end point was to compare the number of episodes of RAD exacerbation before and after Prevnar-20. Sample size calculated by using Open Epi CDC calculator. A P-value of less than 0.05 was considered to indicate statistical significance. Statistical analyses were carried out with the use of SPSS software, version 28.0.

Results: Significantly fewer RAD episodes were reported for Cases than Controls. All the independent sample tests gave results like primary analysis. The Chi square test was statistically significant for fewer RAD episodes in cases than controls (p-value <0.05). The overall effectiveness for Prevnar-20 in prevention of RAD was higher among cases as compared to controls. Similarly, patients who received Prevnar-20 had less ER visits and hospitalization for RAD exacerbations as compared to controls.

Conclusion: It was shown that children who were given Prevnar- 20 had significantly fewer episodes of RAD, less wheezing, albuterol prescriptions, ER visits and subsequent hospitalizations statistically and clinically. We will continue to provide this valuable vaccine in our clinics.

Keywords: Prevnar-20; reactive airway disease; pediatric asthma; reversible bronchoconstriction; reactive airway disease exacerbation; daycare attendance; smokers; wheezing; albuterol

Introduction

Reactive Airway Disease (RAD) can be defined as reversible bronchoconstriction in the lower respiratory tract resulting from smooth muscle contraction in the bronchial walls, edema and infiltration of inflammatory infiltrates, increased mucus production [1].

Acute exacerbation of RAD in the pediatric population is distressing not only to the patient and their families, but also to the healthcare system. Pneumococcal vaccine is a CDC recommended vaccine approved for administration among patients 4-dose series starting at 6 weeks of age up to 5 years of age or 5-18 years of age only if high risk patients [2]. Additional dose of pneumococcal vaccine is recommended in patients with asthma, diabetes, Human Immunodeficiency virus (HIV) and immunocompromised, patients with cerebrospinal fluid leakage, chronic heart disease, chronic lung disease, cochlear implant, sickle cell disease, asplenic patients, and chronic renal failure [3]. We start series of pneumococcal vaccine in the United States at 2 months of age. Previously, we were

administering PCV-13 which is a pneumococcal vaccine against 13 strains. CDC approved Prevnar-20 for pediatric patients which is an updated version of pneumococcal vaccine, has similar structure and formulation but covering 20 strains of S. Pneumoniae in April 2023 [4,5]. We started administering Prevnar-20 at the University of Texas Medical Branch (UTMB) in Galveston, TX in September 2023 including those patients who received PCV-13 previously.

The earliest age at which asthma can be diagnosed is 4-years of age hence all other wheezing episodes are diagnosed as RAD. Most common cause of RAD exacerbation is respiratory viral illnesses [6]. We are conducting this study in hopes of seeing some evidence in our institution in prevention of acute exacerbation of RAD in children after receiving Prevnar-20 vaccine. If we obtain meaningful results, our study may serve as a steppingstone for future studies. By preventing the number of episodes of acute exacerbation of RAD, we will be making a difference for patients and their families. We aimed to assess the effectiveness of Prevnar-20 vaccine against

hospitalization for acute exacerbation of RAD among children younger than 4 years of age.

Methods

Study Design

This is a retrospective, unmatched case-control study done at UTMB to assess the effectiveness of Prevnar-20 against acute exacerbation of RAD requiring health care visits in children less than 4 years of age. We preferred unmatched case control study due to availability of sample size to avoid selection biases from matching if done incorrectly. Prevnar-20 was approved by CDC in June 2023. The use of Prevnar-20 has increased nationwide since June 2023, so it was important to include both case and control patients concomitantly. It was implemented at UTMB in September 2023. The study protocol was approved by the IRB committee (24-0186). This study was based on chart reviews and only those patients were included who had voluntary consent to participate in research in their chart.

Patients and Settings

In this study, we included children younger than 4 years of age who required pediatric acute care visit for RAD exacerbation at UTMB campuses and community-based clinics in the South of Houston, TX between September 2023 to September 2024. Cases consisted of patients who received at least 1 dose of Prevnar-20, and the control group included patients who received PCV-13 during the study period at one of the UTMB campuses. We excluded those patients who are older than 4 years of age, declined immunization per parental preferences, immunization record not available on Electronic Medical Record (EMR) and those who do not have consent for voluntary participation in research in the EMR.

Data Collection

We collected data on immunization status of pneumococcal vaccine, number of episodes of RAD exacerbation requiring Emergency Department (ED) visits or hospitalization, how many times albuterol was prescribed in the past 12 months, day care attendance, family history of asthma, secondhand smoking exposure in household, risk factors for RAD exacerbation and whether number of these episodes decreased after administering Prevnar-20.

Outcome and Exposure measures

The primary end point was the number of episodes of acute exacerbation of RAD after receiving prevnar-20 immunization. Secondary end point was to compare the number of episodes of acute exacerbation of RAD before and after Prevnar-20 vaccinated patients. The treatment exposure was pneumococcal vaccination status among both case and control patients at least 2 months before the date of the pediatric acute care (ED or urgent care) visit.

Sample size and statistical Analysis

Sample size calculated by using Open Epi CDC calculator [7], with 2-sided confidence of 95%, power 80%, ratio of controls to cases 2:1 and percent of controls exposed 50.7%, percent of cases 75.6% giving Odds Ratio of 3.0128 with calculated sample size to consist of 50 cases 100 controls. A P-value of less than 0.05 was considered to indicate statistical significance. Statistical analyses were carried out with the use of SPSS software, version 28.0 (UTMB licensed version).

Results

We enrolled 50 case patients (33.3%) and 100 control subjects (66.7%) who had received ≥ 1 dose of Prevnar-20.

Among cases, 62% (31) patients were males, and 38% (19) patients were females. 2% (1) patients were 6 months –1 year of age, 94% (47) patients were 1-2 years of age, 4% (2) patients were 2-3 years of age. 22% (11) patients were Caucasian, 24% (12) patients were African American, and 54% (27) patients were Hispanic. 32% (16) patients had a family history of asthma, and 68% (34) patients did not. 20% (10) patients attended daycare while 80% (40) patients were staying at home. 6% (3) Patients had someone smoking in the household whereas 94% (47) patients reported not being around smokers.

Among controls, 54% (54) patients were males, and 46% (46) patients were females. 9% (9) patients were 1-2 years of age, 41% (41) patients were 2-3 years of age, 48% (48) patients were 3-4 years of age. 28% (28) patients were Caucasian, 24% (24) patients were African American, 3% (3) patients were Asian, and 45% (45) patients were Hispanic. 24% (24) patients had family history of asthma, and 76% (76) patients did not. 37% (37) patients attended daycare 63% (63) patients were staying at home. 11% (11) Patients had someone smoking in the household whereas 89% (89) patients reported not being around smokers.

Among cases, 68% (34) patients received 1 dose of Prevnar-20 along with other pneumococcal vaccine, 26% (13) patients received 2 doses of Prevnar-20 along with other pneumococcal vaccine, 6% (3) patients received 3 doses of Prevnar-20 along with other pneumococcal vaccine or 3 doses of Prevnar-20 by itself. Among controls, 24% (24) patients received up to 3 doses of pneumococcal vaccine, 73% (73) patients received 4 doses of pneumococcal vaccine, 3% (3) patients received 5 doses of pneumococcal vaccine. Mean number of doses of Prevnar among cases was 2.36 with standard deviation 0.663 whereas mean number of doses of PCV 13 among cases were 3.69 with standard deviation 0.734.

Among cases, 80% (40) patients had wheezing and required albuterol, and 20% (10) patients did not wheeze. Among controls, all of them (100%) had wheezing and required albuterol. Among cases, 6% (3) patients had >3 episodes of RAD, 94% (47) patients had <3 episodes of RAD. Among controls, 33% (33) patients had >3 episodes of RAD, 67% (67) patients had <3 episodes of RAD (**Figure 1**).

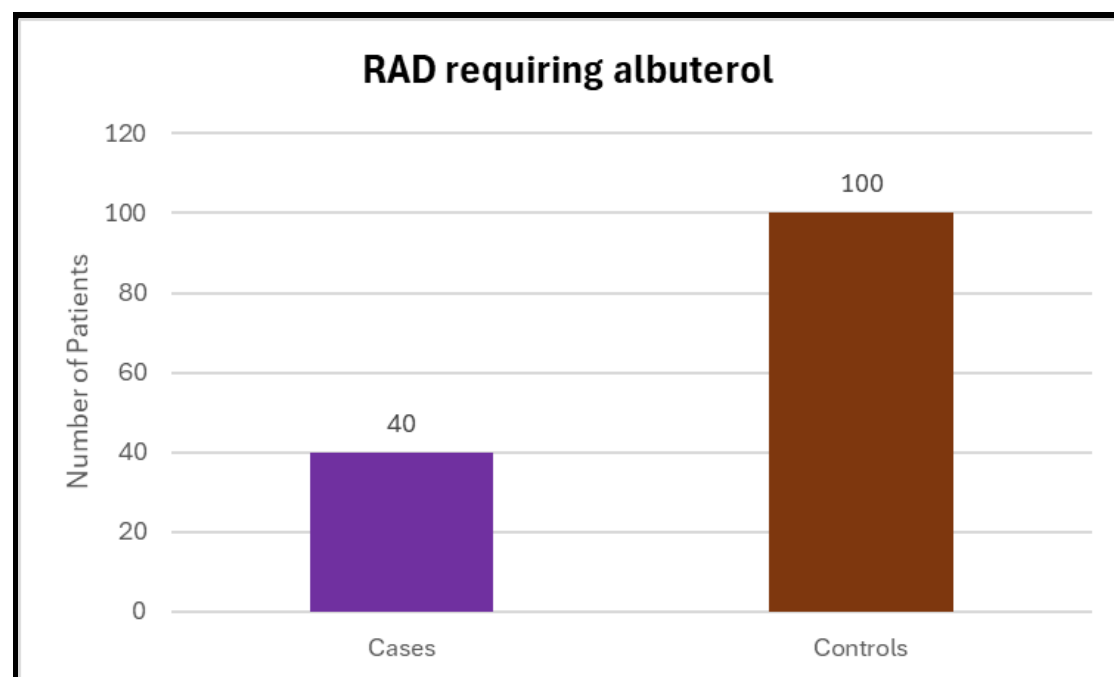


Figure 1: Number of patients with RAD requiring albuterol among cases and controls.

Among cases, 32% (16) patients required ER visit for RAD and 20% (10) of them were hospitalized for acute hypoxemic respiratory failure due to exacerbation of RAD. Among controls, 23% (23) patients required ER visit for RAD and 16% (16) of them were hospitalized for further management (**Figure 2**).

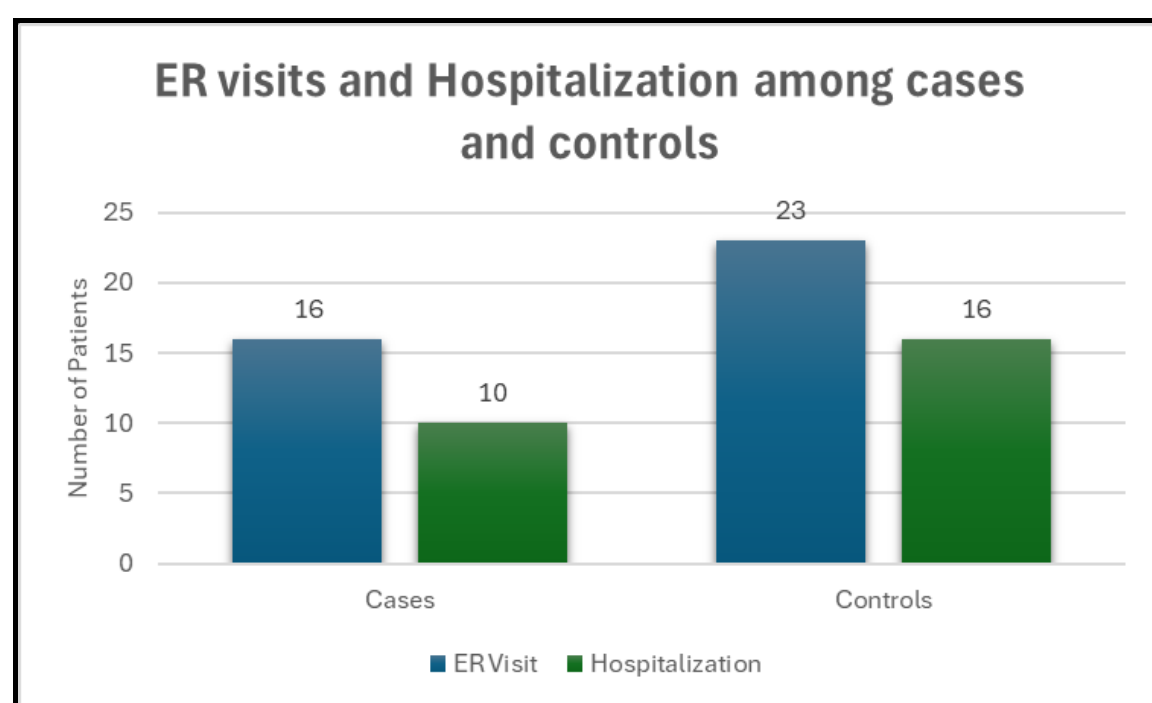


Figure 2: Number of patients requiring ER visits and Hospitalization among cases and controls

Given the wheezing, ER visits and hospitalization, 14% (7) were high risk patients and 68% (34) were low risk patients among cases whereas 48% (48) were high risk patients and 52% (52) were low risk patients among controls (**Table 1**).

Table 1: Table showing comparison among cases and controls

	Cases (Pneum-20) n=50	Controls (PCV-13) n=100
Family history of Asthma	16	24
Day care Attendance	10	37
Smoking in the Household	3	11
Wheezing requiring albuterol	40	100
<3 episodes of RAD	47	67
>3 episodes of RAD	3	33
ER Visit	16	23
Hospitalization	10	16

Significantly fewer RAD episodes were reported for Cases than Controls. All the independent sample tests gave results like primary analysis. Chi square test was statistically significant for fewer RAD episodes in cases than controls (p-value <0.05).

Patients who received Prevnar-20 had less ER visits and hospitalization for RAD exacerbations as compared to controls.

Discussion

Genetic and environmental factors play a significant role in the development of RAD and subsequently asthma. Observational studies have shown that children with severe viral lower respiratory tract infections in early childhood have a higher rate of developing asthma later in life [6]. Additionally, RAD is mostly exacerbated by viral respiratory infections but we noticed fewer episodes of RAD in patients with Prevnar-20 with additional coverage among some strains that were not previously covered by other pneumococcal vaccine. Patients who were immunized against Strep. Pneumoniae with Prevnar-20 may have decreased the risk of RAD exacerbation due to immunity to this bacterium.

Some of the previous studies demonstrated that day care attendance was associated with increased risk of reactive airway disease and subsequently asthma later in life due to exposure to respiratory infections early in life and subsequent wheezing among at risk patient populations whereas other studies consider daycare as a protective factor against developing asthma [8,9]. In our study, there was no correlation between day care attendance and exacerbation of RAD as many of our study participants were not enrolled in childcare centers. From a survey conducted in United States from 1980 to 2017, family history of asthma increases the risk of development of RAD of asthma in the child given the complex interaction between genetic and environmental factors [10]. However, in our study, the majority of our patients in both groups did not have a family history of asthma which could be because of the immunization status optimizing the role of environmental factors in triggering exacerbation of RAD.

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Various meta-analysis has shown secondhand smoke exposure and exacerbation of asthma/RAD [11]. In our study, there was no association between smoke exposure and RAD. It could be either from under-reporting to prevent stigmatization among different ethnic groups or since it was an unmatched case control study, we did not recruit enough patients with smoking exposure to give us a meaningful correlation.

Risk groups were categorized as high and low risk groups. Low risk group was defined as patients with RAD, who were prescribed albuterol but had <3 episodes of RAD exacerbation. High risk group was defined as patients with RAD, who were prescribed albuterol but had 3 or more episodes of RAD exacerbation or required hospitalization and needed oxygen supplementation. The cases involve a higher number of patients from the high-risk group. Among the controls, most of the patients were in the low-risk group.

Average number of doses was lower in cases than controls which means a smaller number of doses of Prevnar-20 are required as compared to PCV 13 and statistically significant fewer episodes of RAD are noted in cases than controls with less wheezing, albuterol prescription, ER visits and subsequent hospitalization. We started administering Prevnar before fall-winter time in 2023, we were able to see significant differences among 2 groups statistically as well as clinically. Prevnar may be a beneficial adjunctive therapy in the care of RAD patients to reduce exacerbations. A similar effect was observed in patients who received Prevnar-20, which offers broader coverage against additional strains [12].

Conclusion

Administration of Prevnar-20 may help to reduce the frequency and severity of RAD exacerbations. It was shown that children who were given Prevnar- 20 had significantly fewer episodes of RAD, less wheezing, albuterol prescriptions, ER visits and subsequent hospitalizations. We will continue to provide this valuable vaccine in our clinics and hope that many other clinics have adopted the same practice.

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