# Frequency of Acute Otitis Media in Children Under 24 Months of Age Before and After the Introduction of the 10-valent Pneumococcal Conjugate Vaccine Into the National Immunization Program in Chile

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**Background:** *Streptococcus pneumoniae* is the leading cause of acute otitis media (AOM). Ten-valent pneumococcal conjugated vaccine (PCV-10) was introduced to the Chilean National Immunization Program (NIP) in 2011. The aim of this study was to estimate the frequency of AOM in children <24 months of age attending the emergency department (ED) of Hospital Sótero del Río (HSR) 4 years before and 4 years after the introduction of PCV-10 in the Chilean NIP.

**Methods:** Register-based nested case-control study. Cases (n = 1907) were all children <24 months of age with a clinical diagnosis discharge of AOM at the ED of HSR, and controls (n = 244,334) were all other children <24 months of age attended at the same ED in the same time period, with any other discharge diagnosis. The data were obtained through HSR Statistical Service.

**Results:** In the study period, there was a mean of 30,695 children <24 months managed each year at the ED of HSR. The percentage with AOM in the prevaccine period was 0.94% and in the postvaccine period was 0.62%, respectively ($P = 0.026$). Exposure to the PCV-10 was associated with a decreased risk to develop AOM in children <24 months, with an odds ratio of 0.659 (95% confidence interval: 0.60–0.72).

**Conclusions:** Our study showed a significant decrease in the percentage and risk of AOM in children <24 months of age who visited the ED of HSR after implementation of PCV-10 in the NIP in Chile.

**Key Words:** acute otitis media, pneumococcal vaccine, pediatrics

(*Pediatr Infect Dis J* 2018;37:132–134)

Acute otitis media (AOM) is one of the most common infectious diseases of bacterial etiology in pediatric population, especially in children younger than 2 years of age.[1]

Etiologic studies carried out worldwide have demonstrated that *Streptococcus pneumoniae* is the leading cause of AOM.[2–5] Microbiologic studies made by our group in children with AOM in Santiago, Chile (2001 and 2006), demonstrated the presence of *S. pneumoniae* in middle ear fluid in 40% of the cases and *Haemophilus influenza* in 29%.[3,6]

There are 2 available types of pneumococcal conjugated vaccines (PCVs): 10-valent (PCV-10) and 13-valent (PCV-13), both supported by clinical trials that have proven their efficacy against pneumococcal invasive infections, further demonstrating immunogenicity and safety.[7–12] The actual World Health Organization recommendation is to include anti pneumococcal vaccine in all countries, reaching a national immunization coverage ≥ 90%.[13] In Chile, PCV-10 was introduced into the Chilean National Immunization Program (NIP) on January 2011 with a 3-dose schedule at 2,4 and 6 months of age with a booster dose at 12 months. One year later, the scheme was modified, eliminating the 6 months dose. The World Health Organization reported a national coverage for the PCV-10 of 82 % in 2012, 79% in 2013, 92% in 2014 and 90% in 2015.[14]

The efficacy of the pneumococcal vaccine to prevent AOM was shown in a study developed in the Czech Republic in 2006, decreasing the incidence of AOM in 33.6% in the group that received pneumococcal vaccine.[15]

The aim of this study was to estimate the frequency of AOM in children <24 months of age attending at the emergency department (ED) of Hospital Sótero del Río (HSR) before and after the implementation of PCV-10 in the Chilean NIP with a total period of observation of 9 years.

## METHODS

### Overall Study Design

This was a register-based nested case-control study. Population included all children <24 months of age who consulted at the ED of HSR, from January 1, 2007, to December 31, 2015 (n = 276,254). The cases were children <24 months with discharge clinical diagnosis of AOM. They were identified according to the CIE-10 code: H.65 nonsuppurative otitis media, H.66 suppurative otitis media and nonspecify otitis media and H.67 otitis media in diseases classified in other code. The controls were all other children <24 months attended at the same ED in the same period of time, with any other discharge diagnosis. The information was obtained from the HSR Statistical Service. The study was approved by the HSR ethical committee.

### Study Procedures

The exposure to the vaccine was negative in all children <24 months who registered a visit at the ED of HSR in the prevaccine period (2007–2010) and positive in all children <24 months who attended the ED of HSR in the postvaccine period (2012–2015). The year 2011 was considered a transition one (first year of PCV-10 in Chilean NIP); thus, it was considered in the general description of the population but not in the analysis of frequency of AOM before and after NIP implementation.

### Statistical Methods

Continuous data were presented as means and ranges. *t* test was performed to determine if there was a difference in the percentage of AOM cases in the prevaccine period and in the postvaccine period. Percentage was calculated as the (total cases of AOM/total of visits) × 100 for each period.

Accepted for publication July 28, 2017.

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ISSN: 0891-3668/18/3702-0132
DOI: 10.1097/INF.0000000000001722

The effect of the independent variable, exposure to the PCV-10 on AOM, was estimated as odds ratio with 95% confidence interval. A *P* value of <0.05 was considered significant. Statistical analysis was performed using the statistical package Epi Info version 7.2 June, 13 2016 (Centers for Disease Control and Prevention, Atlanta, GA).

## RESULTS

### Description of the Population

The total number of children <24 months who attended the ED of HSR during the study period (2007–2015) were 276,254, with a mean of 30,695 visits/yr (range: 29,358–33,178) with a similar number of visits from 2007 to 2015. The number of children <24 months with clinical discharge diagnosis of AOM attended at the ED of HSR per year was 237 (range: 137–387) (Table 1).

### Frequency of AOM and Risk of AOM in the Study Period

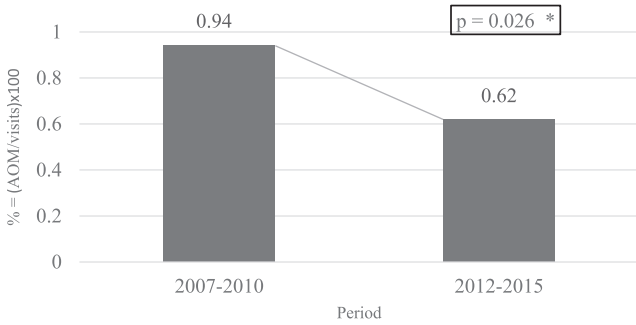
The percentage of children <24 months with clinical diagnosis of AOM was 0.76%, with a range of 0.46%–1.16%. In the prevaccine period, the frequency was 0.94% (range: 0.77%–1.16%), and in the postvaccine period, it was 0.62% (range: 0.46%–0.77%), with a decreased frequency of 32% (*P* = 0.026) (Fig. 1). The frequency of AOM in the transition period (year 2011) was 0.70 %. The mean age of children with AOM was 14 months (range: 0.87–24 months; standard deviation: ± 5.6 months), with a significant difference in the median age in the prevaccine period (13.77 months) and the postvaccine period (14.56 months, *P* = 0.002). The predominant gender was male, without significant difference in both study periods (61.02% and 60.80%, respectively, *P* = 0.92%).

Exposure to the PCV-10 was associated with a decreased risk of AOM in children <24 months with an odds ratio of 0.659 (95% confidence interval: 0.60–0.72) in the exposed population, *P* = 0.01. The percentage of protection had a range of 28%–40%.

**TABLE 1.** Number of Visits and Cases of Acute Otitis Media in Children <24 Months of Age Attending at the Emergency Department of the Hospital Sótero Del Río, Santiago, Chile, Between 2007 and 2015.

| Year | Number of Visits | Number of Cases of AOM | Frequency of AOM (%) |
|---|---|---|---|
| 2007 | 29,844 | 284 | 0.95 |
| 2008 | 29,358 | 227 | 0.77 |
| 2009 | 31,630 | 264 | 0.83 |
| 2010 | 33,178 | 387 | 1.16 |
| 2011 | 31,920 | 223 | 0.70 |
| 2012 | 31,208 | 239 | 0.77 |
| 2013 | 30,207 | 196 | 0.65 |
| 2014 | 29,488 | 137 | 0.46 |
| 2015 | 29,421 | 173 | 0.59 |

Frequency = (number of cases of AOM/number of visits) × 100.




*Difference between percentage of cases of acute otitis media for the pre vaccine and post vaccine period

**FIGURE 1.** Percentage of cases of acute otitis media in children <24 months of age attending at the emergency department of the Hospital Sótero del Río, Santiago, Chile, for the prevaccine period (2007–2010) and postvaccine period (2012–2015).

## DISCUSSION

A study on the efficacy of PCV-10 in Latin American pediatric population was recently published. Between 2007 and 2011, 24,000 infants were enrolled and randomized to receive PCV-10 or hepatitis control vaccine. The children were followed for 4 years. In the study period, there had been 204 (6.9%) episodes of AOM in the PCV-10 group versus 239 (8.8%) in the control group, showing a 16% reduction in the incidence of AOM.[16] These results are consistent with our study showing a statistically significant difference in the frequency of AOM before and after the PCV-10 introduction in the NIP.

Diagnostic error on AOM generally leans toward over-diagnosis; this could complicate the measurement of the vaccine effect on the frequency of AOM, when the diagnosis is clinically defined as in our study. However, this diagnostic error should be stable over time, a situation that was previously shown in 2 studies conducted by our group, comparing the clinically AOM diagnosis made in the ED and the etiologic AOM diagnosis made in the Otorhinolaringology Department by ear tympanic fluid study, showing an error in diagnosis of 58% and 57.5% in 2001 and 2006, respectively.[6]

Uruguay was the first country that included the PCV-13 in Latin America. The ongoing surveillance, at 2012, documented a significant decline on hospitalization because of pneumonia in children <24 months, with a PCV-13 2 + 1 vaccination schedule.[17] In Chile, a recently published study evaluated the incidence of pneumonia in hospitalized children <24 months of age in a pediatric hospital in Santiago, before and after the introduction of the PCV-10 into the NIP in Chile, showing a significant decrease of this pathology,[18] similar to reported in Brazil.[19]

With the use of the PCV, there have been changes on the distribution of pneumococcal serotypes for invasive pneumococcal disease. In Chile, after the implementation of the PCV-10, there has been a decline of the serotype 1 and 14 and an increase in cases related to serotype 3 and 19A, the latest from 6% for the period 2007–2010 to 23% in 2014, similar to has been observed in other countries that use PCV-10.[20,21]

In the 5 years after the implementation of the vaccine in the Chilean NIP, we have seen a significant reduction in the AOM. The next step is to study the incidence and etiology of AOM through tympanic puncture, analyzing the relative role of *S. pneumoniae* and the representation of each serotype in AOM in an era of pneumococcal vaccination.

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