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Early impact of 10-valent pneumococcal conjugate vaccine in childhood pneumonia hospitalizations using primary data from an active population-based surveillance

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ABSTRACT

Background: In Brazil, 10-valent pneumococcal conjugate vaccine (PCV10) was introduced in 2010 in the childhood routine immunization program. We used primary data to evaluate the effect of PCV10 on the reduction of hospital admissions due to community-acquired pneumonia (CAP).
Methods: Active population-based surveillance studies on pneumonia hospitalizations in children aged <36 months were conducted before and after PCV10 introduction in Central Brazil. The surveillances comprised all 17 pediatric hospitals of the study area, which provide assistance for public and private health insurances. Linear regression was performed to detect any trend in pneumonia monthly rates previously to vaccine introduction. PCV10 post-vaccination impact (Nov/2011 to Oct/2013) on clinical and X-Ray confirmed pneumonia was estimated as the relative and the absolute reduction (prevented burden) in pneumonia admission rates, taking as baseline the pre-vaccination period (May/2007 to Apr/2009).
Results: Overall, males presented higher rates of pneumonia hospitalization, compared to females. The relative rate reduction for clinical and X-Ray confirmed pneumonia was 13.1%, and 25.4%, respectively for children aged 2–23 months. The highest prevented burden was observed in age-groups 2–11 months, respectively 853/100,000 (from 6788/100,000 to 5935/100,000), and 729/100,000 (from 2871/100,000 to 2142/100,000), for clinical and X-Ray confirmed pneumonia.
Conclusions: This study provides evidence for the impact of PCV10 in clinical and X-Ray confirmed pneumonia in routine vaccination program in Brazil, after 3 years of vaccine introduction. Extended follow-up studies should confirm the benefit of vaccination through herd effect given the high burden of pneumonia in our setting.

1. Introduction

Pneumonia is the leading cause of morbidity and mortality in infants worldwide, especially in developing countries. Despite the advances in new preventive interventions and case-management strategies in the last decade [1], high rates of pneumonia hospitalizations and deaths in infants are still reported in many countries [2]. In 2011, 120 million episodes of childhood pneumonia were globally estimated, with 14 million hospitalizations, and 1.3 million of deaths, mainly in children under 2 years of age living in low and middle-income countries [3]. Identification of pneumonia etiology may be challenging as few children develop bacteremic

Abbreviations: CAP, community-acquired pneumonia; PCV, pneumococcal conjugate vaccines; PCV7, 7-valent pneumococcal conjugate vaccine; PCV10, 10-valent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; NIP, National Immunization Programs; SIH, National Hospitalization Information System; SUS, Unified Health System; LEAP-BRA, Latin American Epidemiologic Assessment of Pneumococcus; CXR, chest radiography; WHO, World Health Organization; CI, confidence intervals.

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illness. However, evidence show that *Streptococcus pneumoniae* is the most frequent etiologic agent of childhood bacterial community-acquired pneumonia (CAP) [4], contributing to 18% of severe cases and 33% of pneumonia deaths [3,5].

Pneumococcal conjugate vaccines (PCV) have been proved to be a highly efficacious intervention to prevent childhood pneumonia [6]. The first pneumococcal conjugate vaccine approved for use in children was pneumococcal 7-valent (PCV7), in 2000 [7]. Two higher-valent PCV – 10-valent (PCV10) and 13-valent (PCV13) – are now widely available for use in children. The number of countries adopting PCV as a part of the National Immunization Programs (NIP) is quickly increasing [8]. In Brazil, PCV10 was introduced in 2010 through the NIP, for all children aged less than 2 years [9]. Previously, PCV7 was only offered for children under risk at pneumococcal disease, which included chronic diseases and immunodeficiency according to the Brazilian Guidelines for Reference Centers to Special Immunobiologics [10].

Several studies have demonstrated the impact of PCV7 in the reduction of pneumonia hospitalizations in children, mostly in developed countries [11,12], but there are few data regarding PCV10 impact. In addition, most PCV10 studies have focused on invasive pneumococcal disease [13–16], although pneumonia is responsible for most of the morbidity and mortality burden of pneumococcal infections.

Primary data from population-based surveillance is crucial to estimate disease burden and therefore evaluate vaccination impact [17,18]. However, few population-based active surveillance studies on pneumonia have been performed to generate evidence for immunization policies and programs, especially because they are expensive and of significant operational complexity [19–21].

The impact of PCV10 on pneumonia hospitalizations in Brazilian children has been analyzed through secondary data obtained from the National Hospitalization Information System (SIH) [22–24]. However, SIH comprises only cases hospitalized to the Unified Health System (SUS), the Brazilian public health system, lacking information from users of the private health sector. So far, PCV10 impact on pneumonia hospitalizations in childhood using primary data from both public and private healthcare sectors has not yet been reported.

In this study, we analyzed primary data obtained from population-based surveillance of hospitalized children with pneumonia, before and after 3 years of PCV10 introduction into the national immunization schedules. We aimed to assess the impact of PCV10 vaccination program on the reduction of pneumonia hospitalizations rates in infants targeted by the immunization program in Central Brazil.

2. Materials and methods

2.1. Study location and design

The investigation was conducted in Goiânia municipality, capital of Goiás state, located at the Central-Western Region of Brazil. The population of Goiânia for the year 2012 was estimated as 1.333.767 inhabitants, of which 52.562 were children under 3 years of age [25]. In Brazil, the healthcare system is structured including both public and private sector. Although the public system – SUS – offers free and universal assistance to all population, it is estimated that approximately 70% of the population uses such system [26,27]. In Goiânia, 67% of the population uses SUS [24].

Anticipating the introduction of PCV10 in Brazil, in May/2007 we started a two-year population-based surveillance study of children with pneumonia, completed in April/2009. Further details on the study methods of the "*Latin American Epidemiologic Assessment of Pneumococcus*" Study (LEAP-BRA Study), which provides baseline incidence estimates of pneumonia prior to PCV10 introduction, are described elsewhere [28]. In the present investigation, we carried out a post-PCV10 population-based surveillance of children with pneumonia with the same methodology used in the LEAP-BRA Study, to enable comparison between the pre- and post-vaccination periods. The post-PCV10 surveillance study took place from November/2011 to October/2013, being initiated 17 months after PCV10 introduction into the routine vaccination schedule. Both pre- and post-PCV10 studies were prospective population-based surveillance studies, in which primary data on pneumonia hospitalizations were obtained through daily active search of pneumonia cases in children less than 36 months in all the pediatric hospitals in Goiânia municipality.

The study protocol was approved by the Ethics Committee of the Federal University of Goiás, Goiânia, Brazil (protocol # 100/11). Informed consent was obtained from each parent/guardian prior to performance of any study procedures.

2.2. Study population and case ascertainment

The study population included children aged 2–35 months living in Goiânia, which is the target age-group for PCV10 vaccination. The municipality of Goiânia has 17 pediatric hospitals, of which four are exclusively funded by the SUS, providing care for patients using the public healthcare system only, whereas the remaining 13 hospitals provides care through both the public and private healthcare systems.

Target population and case ascertainment procedures were the same for both the pre- and post-PCV10 pneumonia surveillance studies. Children referred to hospital admission in any of the 17 pediatric hospitals of the municipality with signs and symptoms of pneumonia were eligible for enrollment. All children presenting cough and/or difficulty breathing were assigned as suspected CAP by a pediatrician, according to Brazilian guidelines of clinical pneumonia definition [29,30]. Suspected CAP cases were screened by trained research assistants who conducted daily active case search for pneumonia diagnosis in medical charts.

All CAP cases screened that were given a diagnosis other than pneumonia during hospitalization by the attending pediatrician, or did not take the CXR within 72 h of admission were excluded from the study. Also, patients who did not comply with inclusion criteria but had been inadvertently screened (i.e. target age group, place of residency) were excluded.

Fig. 1 shows a flowchart depicting the case ascertainment of pneumonia cases in both pre- and post-PCV10 introduction surveillance studies.

2.3. Data collection

Information on hospitalized children with pneumonia included in the study was collected by trained field-nurses through medical charts review and interviews of parents or legal guardians. Data collection included birth and admission date, gender, length of stay, day-care attendance, preterm birth (before 37 weeks of pregnancy are completed), and patient discharge status (alive/death). Data entry was performed using Smartphones by means of a software (*e*-Pneumo) specifically developed for this study [31], with secure transmission of encrypted data over the internet and server authentication. CXR film images were photographed and converted to high-resolution images following the WHO guidelines for standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children [32].