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Frequency of complications and the effects of pneumococcal vaccination in young children with acute respiratory tract infection

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ABSTRACT

Background: Acute respiratory infection (ARI) is the most frequent reason for children being seen by doctors worldwide. We aimed to estimate the frequency of complications in children aged 6–23 months during ARI episode and to evaluate risk factors present on recruitment associated with complications after the universal implementation of pneumococcal vaccine (PCV10) in our region.

Methods: This prospective cohort enrolled children who had shown ARI for up to 7 days and who were subsequently followed up 14–21 days after, in Salvador, Brazil. Data on recruitment were registered. The vaccine card was personally checked. Complication was defined when hospitalization, pneumonia or acute otitis media (AOM) were informed during the follow-up visit. Pneumonia and AOM were diagnosed by a doctor. Multiple logistic regression analysis was performed.

Results: Of 576 children, 422 (73%) returned and 79 (19%; 95%CI: 15–23%) had complications. The mean interval between admission and follow-up was 23 ± 13 days. Pneumonia ($n = 47$; 11%), hospitalization ($n = 28$; 7%), and AOM ($n = 17$; 4%) were reported. Most of the patients presented one complication ($n = 66$; 84%) followed by two ($n = 13$; 16%). Report of fever (92% versus 79%; OR [95%CI]: 2.90 [1.18–7.14]), bird at home (24% versus 14%; OR [95%CI]: 2.13 [1.07–4.26]), ronchi (48% versus 36%; OR [95%CI]: 2.06 [1.16–3.67]) or crackles (17% versus 7%; OR [95%CI]: 2.36 [1.04–5.38]) on auscultation were directly associated with complications whereas PCV10 (59% versus 75%; OR [95%CI]: 0.46 [0.26–0.82]) was inversely associated. Bird at home (OR [95%CI]: 5.80 [1.73–19.38]) and ronchi (OR [95%CI]: 6.39 [1.96–20.85]) were associated with AOM; PCV10 was inversely associated with AOM (OR [95%CI]: 0.16 [0.05–0.52]). Crackles were associated with pneumonia (OR [95%CI]: 2.55 [1.01–6.40]).

Conclusions: One fifth of the children presented complications. PCV10 was independently associated with lower odds of development of AOM. Bird at home and ronchi are risk factors of otitis. Crackles are associated with pneumonia.

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1. Introduction

One of the most common problems that affect children within their first years of life is the occurrence of acute respiratory infections (ARI). It has been reported an adjusted frequency of 6.2 ARI

episodes per child-year among children aged under three years [1]. ARI has been recognized as the main reason for families seeking pediatric assistance [2].

ARI symptoms generally include runny nose, nasal blockage, low-grade fever, cough and the episode can evolve to severe complications, particularly in young children [1,3]. These complications are mainly acute otitis media (AOM), pneumonia, and hospitalization [4–6]. Heikkinen et al. reported the highest frequency for AOM (39.7%), followed by pneumonia (2.4%) and hospitalization (0.8%) in children after an influenza infection [7]. In general,

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malnutrition, inadequate breast feeding and poor immunization have been indicated as the main risk factors involved in the occurrence of complications due to ARI [8]. Pneumococcal infection has been considered as potentially key in the occurrence of ARI complications [9]. There is an increasing frequency of pneumococcal colonization during clinical ARI and the physical changes produced by viral infection in the nasal passages facilitate the isolation or acquisition of pneumococci [9].

We aimed to estimate the frequency of complications in children aged between 6 and 23 months during an ARI episode. We further evaluated risk factors present on recruitment associated with complications after the universal implementation of pneumococcal vaccine (PCV10) in our region.

2. Methods

Our prospective cohort evaluated children aged from 6 to 23 months with symptoms of ARI between September 2009 and October 2013 at an Emergency Department in Salvador, North-eastern Brazil. Children with ARI defined as report of either fever, sneeze, running nose, nasal blockage, or cough for up to seven days were evaluated in the study. Children transferred from other hospitals or reporting previous episode of wheeze were excluded. Parents or legal guardians were invited to sign the written informed consent and, for the eligible children, they were invited to answer a standardized questionnaire.

The questionnaire contained data on the present illness, obstetric, neonatal, family morbidities, as well as the child's lifestyle, and physical examination performed by the emergency pediatrician. Between 14 and 28 days after the study's admission, children returned for a follow up visit and parents or legal guardians answered a questionnaire about the ARI evolution. Complications comprised the following events: hospitalization, pneumonia and AOM. Pneumonia was diagnosed when the child presented cough or fever along with difficulty breathing AND pulmonary infiltrate, consolidation, or pleural effusion in the chest radiograph. AOM was diagnosed when the child presented earache along with tympanic alterations found by otoscopy (bulging position, decreased or absent mobility, abnormal color or opacity, or air-fluid interfaces PLUS distinct erythematous patches or streaks or increased vascularity). Pneumonia and AOM were diagnosed by a doctor.

Nutritional status evaluation was performed by using the software Anthro, version 3.2.2; severe malnutrition, malnutrition, overweight and obesity were defined as z-score for weight-for-height index, respectively, lower than -3 , lower than -2 , higher than 2 , higher than 3 , by using the World Health Organization (WHO) standard [10]. Fever was defined as axillary temperature higher than 37.4°C [11], and tachypnea as respiratory rate (RR) equal to or higher than 50 breaths/min in children aged 6–11 months and RR equal to or higher than 40 breaths/minute in children from 12 months of age onwards [12].

Pneumococcal vaccine (PCV10: Synflorix, GlaxoSmithKline Biologicals, Rixensart, Belgium) was introduced in Salvador, Brazil, in July 2010 for children aged <2 years [13]. Every child included in the study who could have received PCV10 had the vaccine card checked personally by one of the researchers upon recruitment.

Data were entered into Epi Info version 6.04. Data analyses were performed using STATA version 11.0. Descriptive statistics with their 95% confidence intervals (95% CI) were calculated. Independent variables that appeared to be significant in bivariate analyses were firstly included in a robust Poisson model. All the other independent variables and possible interactions were also assessed before the final model to estimate their independent effects on development of complications. The study was approved by the Ethics Committee from the Federal University of Bahia.

3. Results

Among 1154 evaluated children, 504 (43.7%) reported previous episode of wheeze, 11 (1%) came from other hospitals and 63 (5.4%) did not consent. Thus, 576 (49.9%) children were recruited, out of which 422 (73.3%) returned for reevaluation and were included in this study group. Table 1 in the supplementary material shows the comparison of children who returned with children who did not return.

The baseline characteristics of the study group ($n=422$) are described in Table 1. The median age was 10 months (mean 11.4 ± 4.5), 278 (65.9%) were younger than 1 year, 167 (39.6%) were in the range of 6–9 months of age, 206 (48.8%) were males, and 407 (96.4%) were born in Salvador. Most children 391 (92.6%) had been breastfed, and 207 (49%) were still being breastfed at the time of recruitment. The vaccination card could be checked for 384 (91%) children out of which 277 (72.1%) and 168 (43.8%) received PCV10 or influenza vaccine, respectively. The numbers of PCV10 doses that had been given were: 1 dose (36 patients; 13.0%), 2 doses (96 patients; 34.7%), 3 doses (116 patients; 41.9%), 4 doses (29 patients; 10.4%). Presence of environmental factors at home was reported by informants: smokers in the household ($n=80$; 19%), cockroaches 278 (65.9%), insects 271 (64.2%), dust 233 (55.2%), mold 139 (32.9%), rats 108 (25.6%), dogs 93 (22%), bird 68 (16.1%), cats 27 (6.4%) and chicken 15 (3.6%). On physical examination, fever 161 (39.1%), ronchi 162 (38.4%) and tachypnea 99 (23.8%) were the most frequent findings.

The mean interval between admission and the follow-up visit was 23 ± 13 days, median [interquartile range]: 19 [15–27] days. Overall, complications were detected in 79 (19%; 95% CI: 15–23%) patients and this frequency was similar among children aged under 1 year or 1 year and above (17.3% vs. 21.5%; $p=0.3$). Pneumonia ($n=47$; 11.1%), hospitalization ($n=28$; 6.6%) and AOM ($n=17$; 4.0%) were reported. Most of the patients presented one complication ($n=354$; 84%) followed by two ($n=67$; 16%). Overall, 28 patients were hospitalized, 10 with pneumonia and 3 with AOM; the other 15 had other respiratory discomfort.

Tables 2–4 depict the comparison of medical history, environmental factors and clinical presentation of children with or without complications. Differences were significant in bivariate analysis when report of fever, report of wheeze, duration of hoarseness, use of PCV10, chicken or bird at home, ronchi or crackles at physical examination upon recruitment, were all assessed. Table 5 presents the multivariate analysis of factors associated with complications in bivariate analysis. Directly independent association was found between history of fever (OR [95%CI]: 3.30 [1.38–7.89]), bird at home (OR [95%CI]: 1.90 [1.04–3.45]), ronchi (OR [95%CI]: 1.64 [0.99–2.68]) or crackles (OR [95%CI]: 2.62 [1.27–5.41]) at physical examination and complications. Conversely, use of PCV10 was inversely associated with complications. We further assessed the independent association of factors on recruitment in regard to each one of the complications: bird at home (OR [95%CI]: 5.80 [1.73–19.38]) and ronchi (OR [95%CI]: 6.39 [1.96–20.85]) were associated with AOM; PCV10 was inversely associated with AOM (OR [95%CI]: 0.16 [0.05–0.52]). Crackles were associated with pneumonia (OR [95%CI]: 2.55 [1.01–6.40]).

4. Discussion

Our study showed that development of complications during an ARI episode is common among young children as one fifth of them had complications. Pneumonia was the most frequent complication. An environmental factor (bird at home) was an independent risk factor of AOM. On the other hand, PCV10 was independently associated with lower odds of development of AOM. Auscultatory

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