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Distribution of invasive *Streptococcus pneumoniae* serotypes before and 5 years after the introduction of 10-valent pneumococcal conjugate vaccine in Brazil

Maria-Cristina C. Brandileone [a,*], Samanta C.G. Almeida [a], Ruth Minamisava [b], Ana-Lucia Andrade [c]

[a] National Laboratory for Meningitis and Pneumococcal Infections, Center of Bacteriology, Institute Adolfo Lutz (IAL), São Paulo, State of São Paulo, Brazil
[b] Faculty of Nursing, Federal University of Goiás, Goiânia, State of Goias, Brazil
[c] Institute of Tropical Pathology and Public Health, Federal University of Goiás, Goiânia, State of Goias, Brazil

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ABSTRACT

Background: In March 2010, the 10-valent pneumococcal conjugate vaccine (PCV10) was introduced into the routine immunization program in Brazil. We describe the pneumococcal serotypes that caused invasive pneumococcal diseases (IPD) before and after the introduction of PCV10 using data from a national laboratory-based surveillance system.

Method: We compared the prevalence of vaccine types (VT) and non-vaccine types (NVT) of *Streptococcus pneumoniae* in three periods, pre-PCV10 (January/2005-December/2009), early post-PCV10 (January/2010-December/2013), and late post-PCV10 (January/2014-December/2015), by episode in meningitis and non-meningitis cases and by age group. Changes in serotype prevalence in the early and late post-PCV10 periods were determined using pre-PCV10 period as a reference.

Results: A total of 8971 IPD isolates from patients aged 2 months to 99 years were analyzed. In the late post-PCV10 period, the VT-IPD reduction in the 2-month to 4-year age group was 83.4% for meningitis and 87.4% for non-meningitis cases; in the age groups 5–17 years, 18–64 years, and ≥65 years, VT declined by 56.1%, 54.1%, and 47.4%, respectively, in meningitis cases, and by 60.9%, 47.7%, and 53.4%, respectively, in non-meningitis cases. NVT-IPD increased throughout the study period, driven mainly by serotypes 3, 6C, and 19A, which remained the predominant types causing IPD in the late post-PCV10 period.

Conclusion: We observed direct and indirect PCV10 protection against IPD caused by VT and a shift in the distribution of serotypes 5 years after the introduction of PCV10. Continued IPD surveillance is needed to evaluate the sustainability of the high prevalence of serotypes 3, 6C, and 19A, which were not included in PCV10.

1. Introduction

Streptococcus pneumoniae causes invasive pneumococcal disease (IPD), leading to high morbidity and mortality worldwide [1,2]. IPD includes meningitis, bacteremia, and sepsis, with *S. pneumoniae* (Spn) isolated from sterile sites (e.g., cerebrospinal fluid, blood, pleural fluid). After 2000, pneumococcal conjugate vaccines (PCV) were introduced in the national immunization program (NIP) for children in several countries, reducing greatly the IPD caused by vaccine types [3–5]. Moreover, PCV vaccination has contributed to a decrease in IPD in the unvaccinated population through herd protection [5,6].

In March 2010, Brazil introduced a 10-valent pneumococcal conjugate vaccine (PCV10, GlaxoSmithKline vaccines) in the NIP for children, using a schedule of three primary doses at 2, 4, and 6 months of age, plus a booster dose at 12–18 months [7]. At the time of vaccine introduction, a catch-up campaign offered two primary doses plus a booster for children aged 7–11 months and a single dose for children aged 12–23 months [7]. High vaccine coverage with three primary doses (81–94% in 2015) has been achieved since the introduction of PCV10 [8], and a great decline in morbidity caused by IPD has been documented [9,10]. However, studies on the impact of PCV10 in Brazil were conducted shortly after its introduction into the NIP. For instance, a case-control study reported a PCV10 effectiveness of 83.8% against IPD [9]. Another Brazilian study, a time-series analysis of the impact of

* Corresponding author.
E-mail addresses: maria.brandileone@ial.sp.gov.br (M.-C.C. Brandileone), samanta.almeida@ial.sp.gov.br (S.C.G. Almeida), minamisava@gmail.com (R. Minamisava), alssandrade@gmail.com (A.-L. Andrade).

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PCV10, 3 years after introduction of the vaccine, showed a decrease of 41.3% in vaccine serotypes in children aged 2–23 months [10].

Globally, routine PCV immunization has changed the epidemiology of IPD caused by Spn types included in the vaccine, with an increase in non-vaccine types [11,12]. Therefore, monitoring circulating serotypes of Spn after introduction of the vaccine is important to evaluating its impact. The pneumococcal serotype distribution before and/or after the introduction of PCV10 in Brazil has been described only in independent studies, each with a limited number of pneumococcal isolates [13–15]. There has been no comprehensive analysis of serotypes at the national level to evaluate the distribution of serotypes that cause IPD that covers years before and after PCV10 was introduced. In this study, we used data from Brazilian laboratory-based surveillance to assess the distribution of IPD serotypes before and 5 years after the introduction of PCV10 in Brazil.

2. Material and methods

2.1. Study design and population

This was a national laboratory-based surveillance study conducted from January 2005 to December 2015, comprising all age groups, in which the distribution of PCV10 types (VT, serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F) and non-PCV10 types (NVT, serotypes not included in the vaccine) were investigated over three periods of time, pre-PCV10 (January 2005–December 2009), early post-PCV10 (January 2010–December 2013), and late post-PCV10 (January 2014–December 2015), in relation to the introduction of the vaccine into the NIP. We also distinguished between IPD caused by serotypes 3, 6A, and 19A, as these serotypes are included in the PCV13 vaccine, but not PCV10, and serotype 6C, because of its high prevalence in a carrier study conducted in Brazil after vaccination began [16].

2.2. Source of Spn isolates

Spn isolates are sent routinely to the Centre of Bacteriology at Adolfo Lutz Institute (IAL), the Brazilian National Reference Laboratory for meningitis and IPD. IAL receives Spn-IPD isolates collected from the national network of laboratories, coordinated by the Brazilian Ministry of Health. The network encompasses 25 public health laboratories located in each of the Brazilian states (n = 26), covering the whole country, except for the state of Rondonia, which did not send Spn to IAL during the study period. Outside the national network of laboratories, some private hospitals and laboratories also sent pneumococcal isolates to IAL. Isolates were forwarded to IAL, along with the age, gender, and clinical diagnosis

Table 1
Distribution of *S. pneumoniae* serotypes from meningitis cases per vaccination period, Brazil.

Serotypes	Vaccination period					
	Pre-PCV10 2005–2009		Early-post-PCV10 2010–2013		Late-post-PCV10 2014–2015	
	n	%	n	%	n	%
PCV10 types	1311	55.7	653	37.0	113	18.8
1	15	0.6	7	0.4	2	0.3
4	85	3.6	44	2.5	18	3.0
5	29	1.2	5	0.3	12	2.0
6B	192	8.2	102	5.8	10	1.7
7F	53	2.3	46	2.6	10	1.7
9V	64	2.7	31	1.8	5	0.8
14	404	17.2	136	7.7	6	1.0
18C	126	5.4	68	3.9	10	1.7
19F	178	7.6	99	5.6	22	3.7
23F	165	7.0	115	6.5	18	3.0
Non-PCV10 types	1045	44.4	1114	63.0	487	81.2
3	150	6.4	159	9.00	59	9.8
6A	99	4.2	85	4.8	18	3.0
6C	40	1.7	50	2.8	60	10.0
19A	56	2.4	56	3.2	55	9.2
7C	17	0.7	21	1.2	7	1.2
8	21	0.9	44	2.5	18	3.0
9N	37	1.6	39	2.2	15	2.5
10A	49	2.1	48	2.7	19	3.2
11A	49	2.1	43	2.4	24	4.0
12F	94	4.0	141	8.0	23	3.8
13	22	0.9	31	1.8	7	1.2
15A	22	0.9	27	1.5	17	2.8
15B	25	1.1	22	1.3	9	1.5
15C	23	1.0	29	1.6	10	1.7
16F	24	1.0	27	1.5	10	1.7
17F	20	0.9	25	1.4	4	0.7
18A	15	0.6	15	0.9	6	1.0
18B	25	1.1	13	0.7	1	0.2
20	22	0.9	21	1.2	11	1.8
22F	25	1.1	29	1.6	11	1.8
23A	7	0.3	14	0.8	15	2.5
23B	26	1.1	25	1.4	22	3.7
24F	12	0.5	21	1.2	6	1.0
NT*	41	1.7	9	0.5	2	0.3
Other non-PCV10 types	124	5.3	102	5.8	56	9.3
Total	2356	100.0	1767	100.0	600	100.0

* Non-typeable.

Table 2
Distribution of *S. pneumoniae* serotypes from non-meningitis cases per vaccination period, Brazil.

Serotypes	Vaccination period					
	Pre-PCV10 2005–2009		Early-post-PCV10 2010–2013		Late-post-PCV10 2014–2015	
	n	%	n	%	n	%
PCV10 types	934	68.3	702	37.9	256	24.9
1	75	5.5	29	1.6	8	0.8
4	50	3.7	82	4.4	65	6.3
5	64	4.7	85	4.6	62	6.0
6B	122	8.9	80	4.3	14	1.4
7F	35	2.6	110	5.9	38	3.7
9V	65	4.8	54	2.9	15	1.5
14	375	27.4	133	7.2	18	1.8
18C	30	2.2	31	1.7	7	0.7
19F	53	3.9	34	1.8	19	1.8
23F	65	4.8	64	3.5	10	1.0
Non-PCV10 types	433	31.7	1149	62.1	774	75.2
3	76	5.6	189	10.1	109	10.6
6A	33	2.4	71	3.8	26	2.5
6C	9	0.7	65	3.5	49	4.8
19A	46	3.4	92	5.0	138	13.4
7C	4	0.3	11	0.6	9	0.9
8	12	0.9	101	5.5	57	5.5
9N	18	1.3	51	2.8	32	3.1
10A	9	0.7	30	1.6	19	1.8
11A	17	1.2	37	2.0	28	2.7
12F	43	3.2	117	6.3	59	5.7
13	6	0.4	19	1.0	11	1.1
15A	8	0.6	28	1.5	22	2.1
15B	7	0.5	12	0.7	15	1.5
15C	5	0.4	16	0.9	6	0.6
16F	8	0.6	24	1.3	17	1.7
17F	9	0.7	20	1.1	11	1.1
18A	11	0.8	20	1.1	17	1.7
20	8	0.6	49	2.7	24	2.3
22F	17	1.2	49	2.7	27	2.6
23A	5	0.4	14	0.8	13	1.3
23B	10	0.7	12	0.7	10	1.0
24F	6	0.4	13	0.7	12	1.2
NT*	16	1.2	3	0.2	4	0.4
Other non-PCV10 types	50	3.7	106	5.7	59	5.7
Total	1367	100.0	1851	100.0	1030	100.0

* Non-typeable.

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