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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

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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

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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.

Table 3
Distribution and percentage change of *S. pneumoniae* serotypes per age group by clinical diagnosis and vaccination period[a], Brazil.

Age-groups Serotypes	Meningitis								Non-meningitis							
	2005–2009		2010–2013			2014–2015			2005–2009		2010–2013			2014–2015		
	n	%	n	%	Percentage change	n	%	Percentage change	n	%	n	%	Percentage change	n	%	Percentage change
2m-4y																
PCV10 types	580	77.5	192	50.7	−34.7	13	12.9	−83.4	461	81.6	146	41.1	−49.6	15	10.3	−87.4
Non-PCV10 types	168	22.5	187	49.3	119.7	88	87.1	287.9	104	18.4	209	58.9	219.8	131	89.7	387.5
3	14	1.9	21	5.5	196.0	2	2.0	5.8	20	3.5	41	11.5	226.3	17	17.0	380.3
6A	34	4.5	22	5.8	27.7	3	3.0	−34.7	17	3.0	29	8.2	171.5	1	1.0	−66.8
6C	4	0.5	9	2.4	344.1	9	8.9	1566.3	3	0.5	19	5.4	908.0	7	7.0	1218.3
19A	18	2.4	21	5.5	130.3	22	21.8	805.2	24	4.2	42	11.8	178.5	53	53.0	1147.7
other non-PCV10 types	98	13.1	114	30.1	129.6	52	51.5	293.0	40	7.1	78	22.0	210.4	53	53.0	648.6
5-17y																
PCV10 types	244	56.1	112	41.2	−26.6	17	24.6	−56.1	136	74.3	79	54.5	−26.7	18	29.0	−60.9
Non-PCV10 types	191	43.9	160	58.8	34.0	52	75.4	71.6	47	25.7	66	45.5	77.2	44	71.0	176.3
3	23	5.3	25	9.2	73.8	7	10.1	91.9	8	4.4	9	6.2	42.0	6	9.7	121.4
6A	20	4.6	17	6.3	35.9	2	2.9	−37.0	3	1.6	7	4.8	194.5	3	4.8	195.2
6C	7	1.6	8	2.9	82.8	10	14.5	800.6	0	0.0	4	2.8	–	4	6.5	–
19A	12	2.8	7	2.6	−6.7	4	5.8	110.1	6	3.3	10	6.9	110.3	12	19.4	490.3
other non-PCV10 types	129	29.7	103	37.9	27.7	29	42.0	41.7	30	16.4	36	24.8	51.4	19	30.6	86.9
18-64y																
PCV10 types	431	41.7	292	30.1	−27.9	75	19.1	−54.1	279	57.4	363	36.6	−36.2	173	30.0	−47.7
Non-PCV10 types	602	58.3	678	69.9	19.9	317	80.9	38.8	207	42.6	628	63.4	48.8	403	70.0	64.3
3	98	9.5	101	10.4	9.8	49	12.5	31.8	30	6.2	85	8.6	39.0	50	8.7	40.6
6A	42	4.1	40	4.1	1.4	12	3.1	−24.7	9	1.9	25	2.5	36.2	15	2.6	40.6
6C	25	2.4	29	3.0	23.5	38	9.7	300.6	6	1.2	32	3.2	161.6	25	4.3	251.6
19A	22	2.1	23	2.4	11.3	27	6.9	223.4	11	2.3	31	3.1	38.2	49	8.5	275.9
other non-PCV10 types	415	40.2	485	50.0	24.5	191	48.7	21.3	151	31.1	455	45.9	47.8	264	45.8	47.5
≥65y																
PCV10 types	56	40.0	57	39.0	−2.4	8	21.1	−47.4	58	43.6	114	31.7	−27.4	50	20.3	−53.4
Non-PCV10 types	84	60.0	89	61.0	1.6	30	78.9	31.6	75	56.4	246	68.3	21.2	196	79.7	41.3
3	15	10.7	12	8.2	−23.3	1	2.6	−75.4	18	13.5	51	14.2	4.7	36	14.6	8.1
6A	3	2.1	6	4.1	91.8	1	2.6	22.8	4	3.0	10	2.8	−7.6	7	2.8	−5.4
6C	4	2.9	4	2.7	−4.1	3	7.9	176.3	0	0.0	10	2.8	–	13	5.3	–
19A	4	2.9	5	3.4	19.9	2	5.3	84.2	5	3.8	9	2.5	−33.5	24	9.8	159.5
other non-PCV10 types	58	41.4	62	42.5	2.5	23	60.5	46.1	48	36.1	166	46.1	27.8	116	47.2	30.7

[a] Vaccination periods: pre-PCV10 (2005–2009); Early-post-PCV10 (2010–2013); Late-post-PCV10 (2014–2015).

of the patient, which were recorded in a database. For this investigation, the data on IPD-associated serotypes from 2005 to 2015 was extracted in May 2016.

2.3. Microbiology methods

All pneumococcal IPD-associated isolates recovered at local laboratories were confirmed at IAL using standard methods [17]. Spn was serotyped by performing the Quellung reaction with antisera from the Staten Serum Institute (Copenhagen, Denmark). All non-typeable (NT) isolates by Quellung were confirmed by conventional multiplex PCR using 41 primers for the detection of 70 serotypes [18,19].

2.4. Data analysis

Only one invasive Spn from each patient was included in the analysis. Different serotypes isolated >30 days apart from the same patient were considered different IPD episodes.

The distribution of serotypes was analyzed for meningitis and non-meningitis patients and by age group (2 months-4 years, 5–17 years, 18–64 years and ≥65 years) in the vaccine periods. NT isolates were included in NVT group. Changes in the prevalence of VT and NVT for each age group in the early post-PCV10 and late post-PCV10 periods were calculated for meningitis and non-meningitis using the pre-PCV10 period as a reference. The percentage change was used to indicate the change in prevalence of the serotypes between the post-PCV10 and pre-vaccination periods, using the following formula: [(percentage of serotypes in the post-PCV10 period – percentage of serotypes in the pre-PCV10 period/percentage of serotypes in the pre-PCV10 period) * 100]. A positive percentage change expresses an increase in the serotype in the post-PCV10 period, whereas a negative percentage change expresses a reduction in the serotype in the post-vaccination period.

Trends in VT and NVT were described based on the number of isolates per year and plotted for meningitis and non-meningitis cases and by age group: 2–23 months, 2–4 years, 5–17 years, 18–49 years, 50–64 years, and ≥65 years. For serotypes 3, 6A, 19A, and 6C, trends were presented for age groups <18 years and ≥18 years. Isolates from children aged <2 months were excluded because this age group was not targeted to receive the PCV10 vaccine. Since PCV10 was introduced in 2010, individuals in the age groups 2–23 months and 2–4 years were considered the vaccine-targeted population. The data analysis was performed using Stata/SE v13 for Windows (StataCorp, Texas, USA).

3. Results

From January 2005 to December 2015, 10,305 IPD-associated isolates were received at IAL. Duplicate isolates (n = 534, 5.2%), isolates with no information on the patient's age (n = 614, 5.9%), isolates from children aged <2 months (n = 4, <0.1%) and isolates that were not serotyped (n = 182, 1.7%) were excluded from the analysis. Therefore, 8971 IPD isolates from patients aged 2 months

to 99 years were analyzed. Males accounted for 5483 (61.1%) isolates. A total of 4723 (52.7%) isolates were obtained from meningitis cases, with 553 (11.7%) from blood and 4170 (88.3%) from cerebrospinal fluid; 4248 (47.3%) isolates were from non-meningitis cases, with 3730 (87.8%) from blood and 518 (12.2%) from other sterile sites.

Overall, 66 IPD-associated serotypes were identified being 63 in the pre-PCV10 (n = 3723), and 54 in the early post-PCV10 (n = 3618) and 53 in the late post-PCV10 (n = 1630) periods. The distribution of serotypes from meningitis case per vaccination period is shown in Table 1. The prevalence of VT accounted to 55.7%, 37.0%, and 18.8% of meningitis cases in the pre-PCV10 period and early and late post-PCV10 periods, respectively. VT represented 68.3% of non-meningitis cases in the pre-PCV10 period, decreasing to 37.9% and 24.9% in the early and late post-PCV10 periods (Table 2). Among children aged 2 months–4 years, the distribution of VT in the late post-PCV10 period (n = 28) was the following: serotype 5 (n = 6); 23F (n = 5); 6B, 7F, 14, and 19F (n = 4 each); and 18C (n = 1). Serotypes 1, 4 and 9 V were not detected.

Considering NVT in the late post-PCV10 period, serotypes 6C (10%), 3 (9.8%), and 19A (9.2%) were most prevalent in patients with meningitis, and serotypes 19A (13.4%), 3 (10.6%), 12F (5.7%), 8 (5.5%), and 6C (4.8%) were prevalent among non-meningeal cases (Tables 1 and 2).

Table 3 shows the distribution and percentage change in serotypes per age group and clinical diagnosis in each vaccination period. In the vaccine target population (2 months–4 years), reductions in VT in the late post-vaccination period of 83.4% and 87.4% were observed in meningitis and non-meningitis cases, respectively. Considering the age groups 5–17 years, 18–64 years, and ≥65 years in the late post-PCV10 period, 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.

An increase in NVT was notable in both post-PCV10 periods for all age groups for meningitis and non-meningitis cases. In the late post-PCV10 period, relative increase of serotypes 6C and 19A was observed in all age groups in meningitis and in non-meningitis cases; serotype 3 increased in all age groups with both clinical diagnosis, except in older adults aged ≥65 years in meningitis; 6A declined in children aged 2 months–4 years in meningitis and non-meningitis cases, and in the age groups 5–17 years and 18–64 years in meningitis (Table 3).

Trends regarding VT and NVT by age groups in meningitis (Fig. 1) and non-meningitis (Fig. 2) cases showed that two years after vaccination (in 2012), VT decreased in children aged 2–23 months and 2–4 years in both meningitis and non-meningitis cases; after 2013, VT decreased in meningitis cases in all age groups and decreased for individuals <50 years with non-

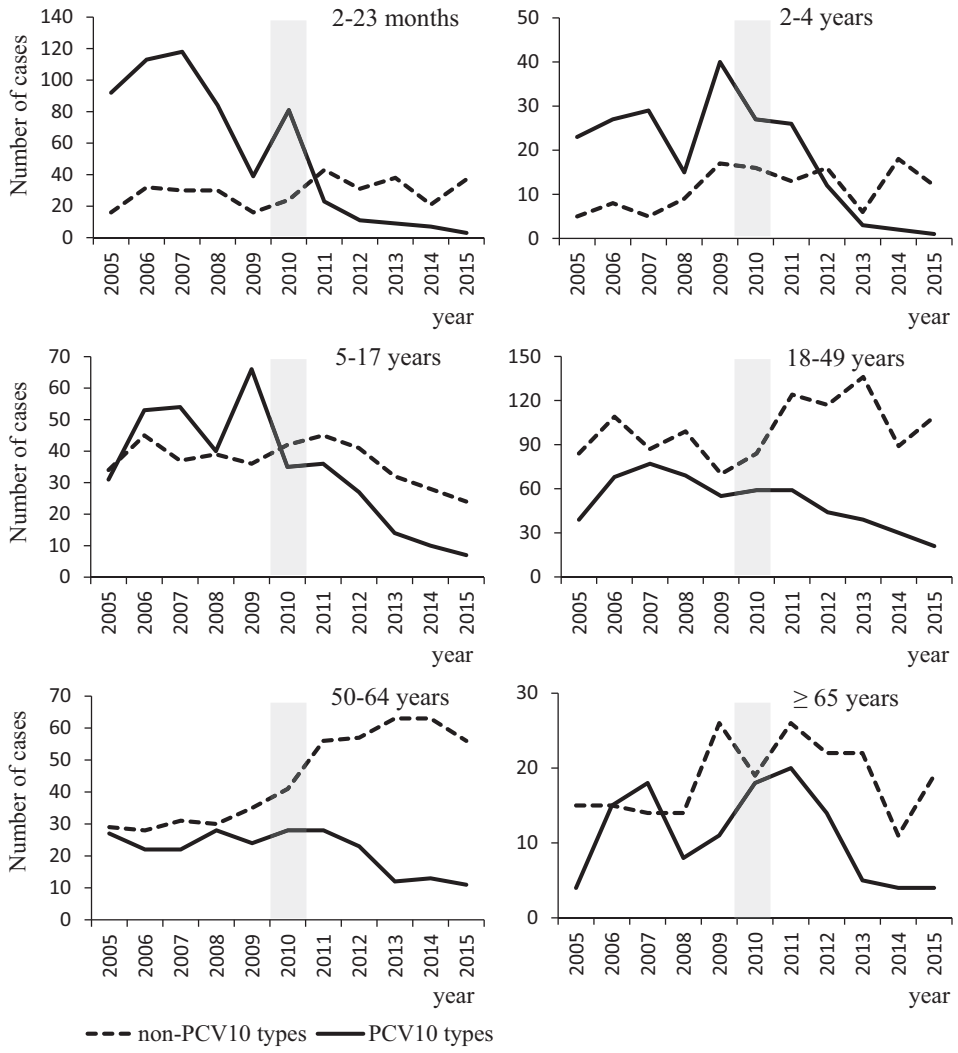

Fig. 1. Trends of *Streptococcus pneumoniae* serotypes from meningitis cases per age group and year; gray area: PCV10 introduction; Note: y-axis between graphics has different values.

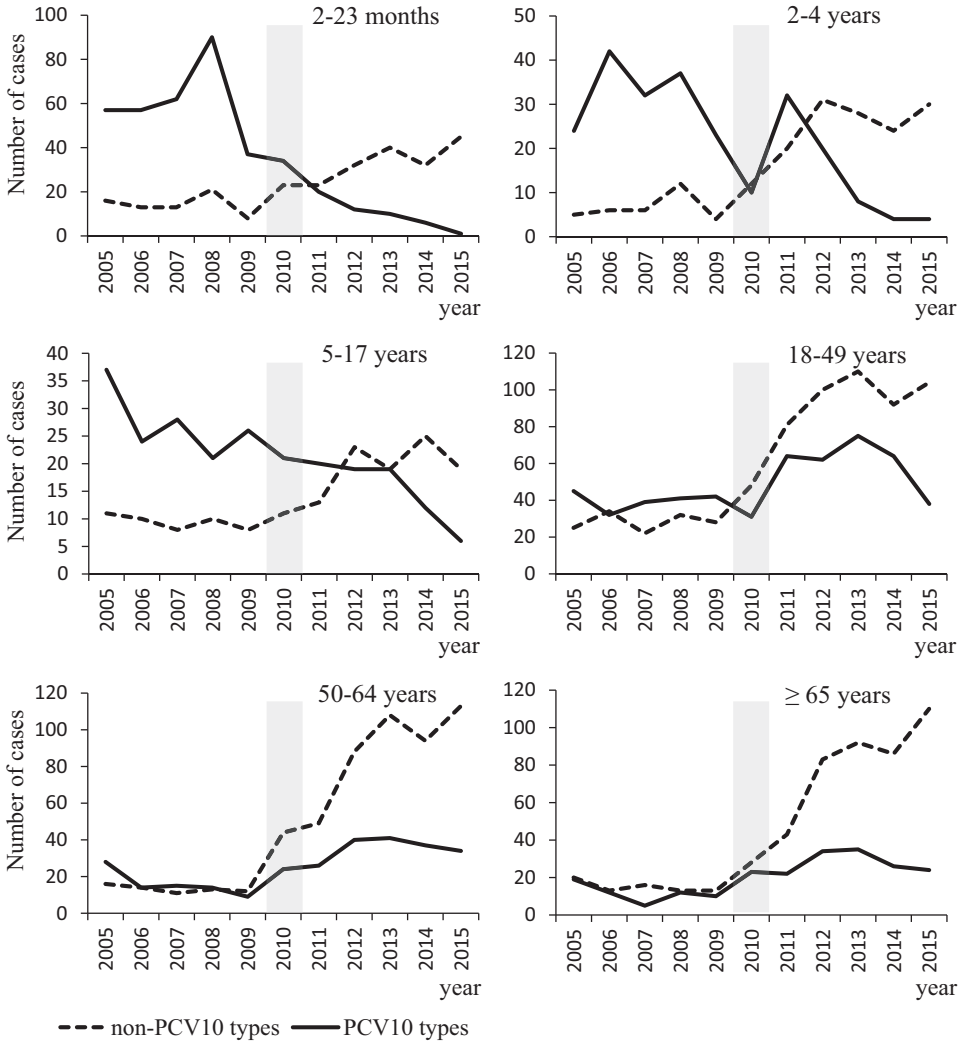

Fig. 2. Trends of *Streptococcus pneumoniae* serotypes from non-meningitis cases per age group and year; gray area: PCV10 introduction; Note: y-axis between graphics has different values.

meningeal episodes. Conversely, after the introduction of PCV10, NVT showed an increasing trend in adults aged 18–49 years and 50–64 years with meningitis, as well as in non-meningitis cases in all age groups, especially among adults aged ≥18 years.

Fig. 3 shows the IPD trends by serotypes 3, 6C, 19A, and 6A by clinical diagnosis in the age groups <18 years and ≥18 years. Through the years, an increasing trend in serotype 3 was observed mostly among patients ≥18 years, with or without meningitis; 19A increased in patients aged <18 years and ≥18 years, especially in non-meningitis cases; and 6C increased especially in patients aged ≥18 years. Trend in 6A suggest a reduction of this serotype in patients aged <18 years after 2013.

4. Discussion

This investigation shows that five years after the introduction of PCV10 into the NIP in Brazil, VT-IPD has declined considerably, changing the profile of serotypes causing IPD. The proportion of meningitis and non-meningitis episodes caused by serotypes 14 and 6B, the most prevalent VT-IPD before vaccination, was small, represented by only a few isolates in the late post-PCV10 period. In addition, rare serotype 1 isolates were identified in the late post-PCV10 period, which may be owing to the natural cyclic fluctuation of this serotype, since serotype 1 was among the most frequent causes of IPD in Brazil during the last decade [20–22]. Among the vaccine target population (children aged 2 months–4 years), VT-IPD declined soon after two years of PCV10 use, reaching almost negligible levels in the years after PCV10 introduction in meningitis and non-meningitis cases.

Importantly, PCV10 vaccination conferred a substantial reduction in VT-IPD in the non-vaccine target population (age groups 18–64 years and ≥65 years), in particular after three years of PCV10 use (2014–2015), leading to substantial herd protection against VT-IPD.

As expected, besides the reduction in VT-IPD, a substantial increase in NVT-IPD was observed, leading mainly to a gradual increase in serotypes 19A, 6C, and 3. Currently, these non-PCV10 types are the major causes of IPD in Brazil. Globally, the NVT-IPD increase after PCV introduction, referred to serotype replacement, might be related to many factors, including antibiotic pressure, pressure of pneumococcal carriage, prevalence of co-morbidities and underlying illness to IPD, and others [11].

In Brazil, an increase in 19A was distinctly detected in the later years of this study in all age groups (2014–2015), when it was the principal cause of meningitis and the second leading cause of non-meningitis episodes. An increase in 19A has been shown in several settings after the introduction of PCV7 or

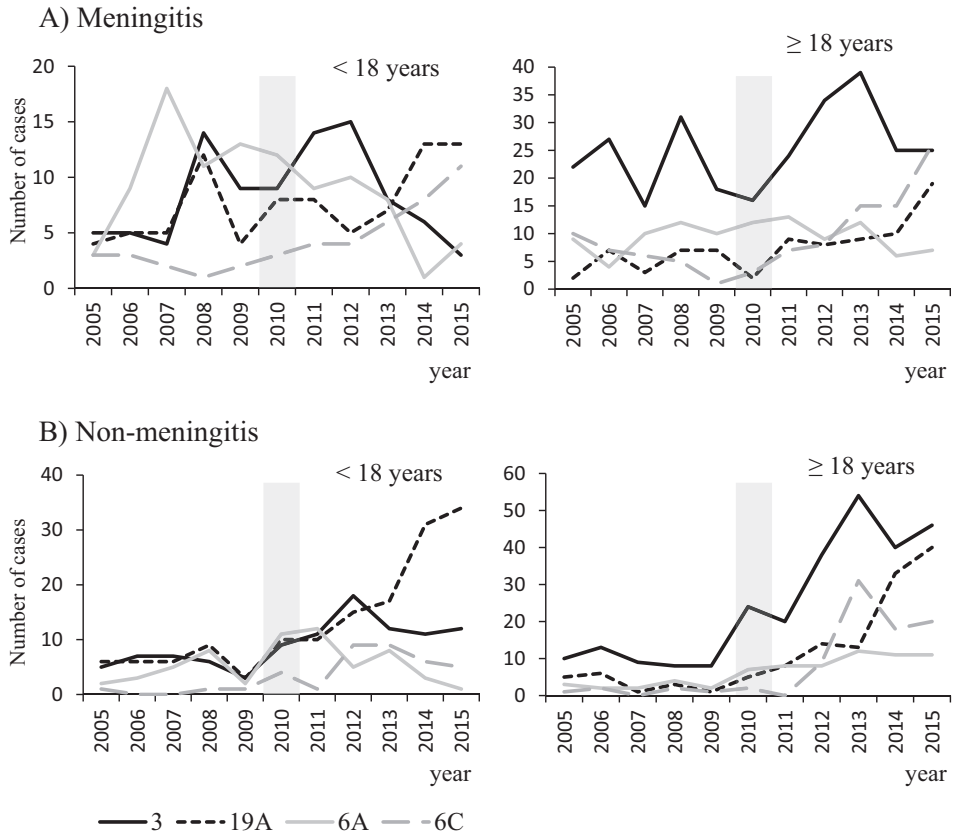

Fig. 3. Trends of *Streptococcus pneumoniae* serotypes 3, 19A, 6A and 6C per clinical diagnosis and age group, per year; gray area: PCV10 introduction; Note: y-axis between graphics has different values.

PCV10 [5,23–25]. In Chile, where PCV10 was introduced in 2010, the overall proportion of 19A-IPD was ≤5% before vaccination, and it increased to 12% in the year 2014; among children aged <2 years, 19A represented <8% of IPD before vaccination, and it increased to 25% in 2014 [26]. Overall, an increase in 19A after PCV7/PCV10 vaccination has been linked to the emergence of antimicrobial-resistant clonal complex 320 (CC320) [27–29]. In Brazil, the emergence of 19A might be attributed to CC320 expansion, at least in part, as genetic characterizations of the 19A strains obtained in this surveillance study revealed a trend of increasing CC320 in the years after PCV10 implementation, with CC320 currently the most prevalent clonal complex of 19A isolates [30–31]. Thus, our findings do not support PCV10 cross-protection against 19A-IPD, in contrast to previous reports from Brazil, Finland, and Quebec (Canada) [9,32–34].

Serotype 6C was rarely identified in the first years of the study (2005–2009), and it increased through the years after vaccination, mainly among children and patients aged ≥18 years. These data suggest that PCV10 does not induce cross-protection for 6C, and consequently does not provide herd protection against 6C-IPD. Emergence of 6C has been reported after PCV introduction in several sites [35–37], and interestingly it high prevalence was previously detected in Brazil in nasopharyngeal carriage surveys among children after three/four years vaccination [16,38].

The increase in serotype 3 found in this surveillance, particularly in patient aged ≥18 years with a diagnosis other than meningitis, was noticeable because this serotype has been largely associated with high mortality of adults [39,40]. In addition, the present data suggest a reduction in 6A-IPD in the vaccine target population, possibly due to cross-protection induced by 6B-VT, as has been reported by others [41,42].

Our findings are in accordance with data from a population-based study conducted in Sweden and recently published that compares the impact of PCV10 and PCV13 in different counties. Naucler et al. reported an overall reduction in VT-IPD incidence in Swedish counties using PCV10 or PCV13, whereas an increase in 6C and 19A and a decline in 6A were observed in counties that used PCV10 [43].

This investigation has some limitations because our data was obtained from a laboratory-based surveillance. In Brazil, meningitis surveillance is high quality, as it is a compulsory notification disease. Thus, the Spn collection was comprised of a large number of isolates from meningitis cases, and relatively few non-meningitis cases, which were underreported. Nevertheless, the number of non-meningitis isolates was large enough to permit a serotype analysis. Furthermore, during the early post-PCV10 period, enhanced laboratory surveillance occurred with the implementation of a case-control study to assess the effectiveness of PCV10 in children in 10 states of Brazil [9]. This led us to analyze the serotype data in the late post-PCV10 period (2014–2015) when the PCV10 effectiveness study was finished. Despite these limitations, the present study is comprised of a large number of IPD isolates recovered throughout the country from the same institutions over the whole study period, suggesting a robust analysis of Spn serotypes, which are highly valuable to monitoring serotype trends.

In conclusion, we observed remarkable direct and indirect PCV10 protection against IPD caused by vaccine strains of Spn 5 years after the introduction of PCV10. In addition, our data shows a shift in the distribution of serotypes, as 3, 6C, and 19A remained the most prevalent types causing IPD in the most recent years of the study.

In 2016, the NIP in Brazil changed the PCV10 vaccine schedule to 2 + 1 doses [44]. Therefore, it is important to improve IPD surveillance to include population-based studies to evaluate the appropriateness of the new vaccination schedule and whether the increase in serotypes 3, 6C, and 19A, which were not included in PCV10, was sustained.

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Authors contributions

Conceived and designed the study: MCCB, SCGA, RM, ALA; statistical analysis: RM, ALA; acquisition of data: MCCB, SCGA; drafting/revision of the manuscript: MCCB, SCGA, RM, ALA.

Conflict of interest

MCCB and ALA received lecture fees and travel grants from GlaxoSmithKline and Pfizer; SCGA and RM received travel grants from GlaxoSmithKline.

Disclaimer

All authors have approved the final version of the manuscript.

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