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Serotype distribution and antimicrobial resistance of *Streptococcus pneumoniae* prior to introduction of the 10-valent pneumococcal conjugate vaccine in Brazil, 2000–2007

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ABSTRACT

This study describes the serotype distribution and antibiotic resistance patterns among 397 *S. pneumoniae* meningitis case isolates recovered in Salvador, Brazil, during the period of 2000–2007, before introduction of the 10-valent pneumococcal conjugate vaccine.

The active hospital-based surveillance showed a decline in the annual incidence rates of pneumococcal meningitis during the period of study, from 1.12 cases to 0.83 cases/100,000 persons for all age groups ($P < 0.001$), with an overall case-fatality rate of 28.6% (113 of 395) for all patients and 41.9% (57 of 136) for those <5 years of age. Serotypes 14 ($n = 55$; 13.9%), 3 ($n = 32$; 8.1%), 23F ($n = 32$; 8.1%), 19F ($n = 31$; 7.8%), 6B ($n = 30$; 7.6%), 18C ($n = 28$; 7.1%), and 6A ($n = 20$; 5%) were the most prevalent serotypes. In patients <5 years the estimated projected coverage of 7-, 10- and 13-valent conjugate vaccines was 74.3%, 75.7% and 83.1%, respectively. Antimicrobial susceptibility testing revealed that 22.1% ($n = 88$) of isolates were non-susceptible to penicillin, 56% were non-susceptible to trimethoprim/sulphamethoxazole, and 29.6% were non-susceptible to tetracycline. Nonsusceptibility to penicillin and cefotaxime was detected solely among serotype 14 isolates ($n = 4$; 1%). This study provides an important baseline to assess the impact of conjugate vaccine implantation on the epidemiology of meningitis due to *Streptococcus pneumoniae* in Salvador, Brazil.

1. Introduction

Streptococcus pneumoniae (pneumococcus) is a major cause of meningitis, pneumonia, and bacteremia, especially among young children and older adults [1]. It is estimated that 1.6–2.2 million children die of pneumococcal disease every year in the world, primarily within developing countries. This death toll includes 0.7–1 million children <5 years of age [2–5].

Introduction of heptavalent pneumococcal conjugate vaccine (PCV7) for infants led to substantial reductions in the incidence of invasive pneumococcal disease (IPD) in the United States and other industrialized countries [2,6]. IPD rates in the vaccine era have also decreased among unvaccinated older children, adults, and elderly persons through reductions in nasopharyngeal colonization and transmission of vaccine-type pneumococci from vaccinated children (herd effect) [7]. However, the increase in the rate of invasive pneumococcal disease (IPD) cases caused by non-vaccine strains has been a concern [6,8]. Although PCV7 continues to effectively decrease the pneumococcal disease burden in the United States, the incidence of IPD caused by serotype 19A strains has increased among vaccinated children, and these strains are often highly resistant to commonly used antimicrobials [9–11].

In Brazil, the national vaccine program using the recently licensed 10-valent PCV (PHiD-CV) vaccine [12] has been imple-

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mented in 2010. This vaccine includes three additional serotypes (1, 5 and 7F) and is projected to cover ≥ 80% of serotypes causing invasive pneumococcal diseases (IPD) in most regions of the world [13,14].

Assessment of changes in serotype distribution potentially related to vaccine introduction requires valid baseline values of both the incidence of IPD and of serotype distribution. Since December 1995, an active hospital-based surveillance for pneumococcal meningitis (PnM) has been conducted in the state reference hospital for infectious diseases in Salvador, Brazil. In this study we describe the pneumococcal serotype distribution and antibiotic resistance patterns among meningitis case isolates from patients referred to that hospital between January 2000 and December 2007. The main objective of our study was to provide a baseline for the interpretation of any changes arising from the future PCV10 vaccination strategy.

2. Material and methods

2.1. Surveillance

Since December 1995, active hospital-based surveillance for pneumococcal meningitis (PnM) has been conducted in Hospital Couto Maia, the state reference hospital for infectious diseases in Salvador, Brazil, which is responsible for about 95% of the meningitis reports from the metropolitan region [15]. Data obtained from the period of 1995–1999 and details of the surveillance study have been described previously [16,17]. For the present analysis, the study population included all patients hospitalized between 1 January 2000 and 31 December 2007 with pneumococcal meningitis, consisted of 34.4% women and 65.6% men aged 0–83 years (mean age 18 ± 19 years). Cases were defined by the isolation of *S. pneumoniae* from cerebrospinal fluid (CSF) specimens and/or by positive latex agglutination test result from a patient with clinical signs and symptoms of meningitis. Patients were identified at the state infectious disease hospital where according to the state health secretary procedures, all suspected cases of meningitis for the region are referred for diagnostic procedures, including routine lumbar puncture and cerebrospinal fluid examination, and to implement isolation precaution protocols. A study team of physicians and medical students reviewed laboratory records five days a week to identify new culture isolations. Demographic and clinical presentations of the patients were collected during interviews or medical chart review.

2.2. Laboratory procedures

S. pneumoniae isolates from CSF cultures were identified by standard bacteriological techniques [18]. From 2000 to 2005, pneumococcal strains were serotyped by the Quellung reaction with type-specific antipneumococcal sera prepared at the Centers for Disease Control and Prevention (CDC). After 2006, the isolates were serotyped by multiplex-PCR as described elsewhere [19,20]. DNA extraction and PCR conditions were performed as described [21]. Isolates with negative or equivocal multiplex PCR results were subjected to Quellung reaction testing for capsular type definition. All isolates identified as serogroup 6 were subjected to *wciN*^{6C}–specific PCR as previously described for the identification of potential serotype 6C and 6D isolates [22]

2.3. Antimicrobial susceptibility testing

The broth microdilution method was performed according to Clinical and Laboratory Standards Institute recommendations [23] to determine susceptibility of the isolates to penicillin (Pen), ofloxacin (Ofl), cefotaxime (Cef), clindamycin (Clin), chloramphenicol (Clo), erythromycin (Eri), tetracycline (Tet), rifampicin (Rif), trimethoprim/sulphamethoxazole (Sxt), and vancomycin (Van) (Sigma–Aldrich, Germany). Quality control was performed by testing *S. pneumoniae* ATCC 49619. Isolates with a penicillin MIC value ≥0.12 μg/mL were defined as penicillin-non-susceptible. Intermediate and resistant isolates were considered non-susceptible.

2.4. Data management

Patients residing in Metropolitan Salvador (population, 3,120,303 inhabitants), which includes Salvador and 12 municipalities, were included for incidence calculations. Incidence calculations were based on the 2000 Brazilian census, provided by the Instituto Brasileiro de Geografia e Estatística without adjusting for population growth [24]. The population in Metropolitan region of Salvador is stable regarding birth cohort and migration rate [24]. Data were entered and managed by Epi Info version 3.5.1 (CDC, Atlanta, GA, USA). The chi-square for trend was applied to compare incidence among the seven years (2000–2007). The chi-square test or Fisher's exact test was performed to compare proportions. Differences were defined to be significant if the two-tailed *P*-value was <0.05.

A generalized linear model was fitted to the log10 transformed penicillin MIC values to evaluate trends over time using SAS® 9.1 for Windows (Cary, NC). Transformations were made to improve normality and to reduce the influence of outliers. The antilogarithm of model predicted values provided a nonlinear trend line through the yearly GMCs.

2.5. Ethics

This project was approved by the Research Ethical Committee of Fundação Oswaldo Cruz and of Hospital Couto Maia.

3. Results

We identified 421 cases of pneumococcal meningitis (PnM) at Hospital Couto Maia, from January 2000 to December 2007. Considering that 236 patients resided within the Metropolitan Salvador, the annual incidence rates of pneumococcal meningitis declined by 26% during the 8-year of surveillance, ranging from 1.12 to 0.83 cases per 100,000 population (mean incidence, 0.9 cases/100,000 persons year for all age groups [$P < 0.001$]) (Table 1). Mean incidence for children < 5 years of age was 4.2 cases/100,000 persons-year (range from 6.4 to 1.78) [$P < 0.001$]. There was an overall case-fatality ratio of 28.6% (113 of 395) for all patients and 41.9% (57 of 136) for those <5 years of age. The majority of the *S. pneumoniae* meningitis cases were patients aged >5 years (254/402; 63.2%), particularly among those aged 5-49 years (227/402; 56.5%) (data not shown). The other pneumococcal meningitis cases comprised children aged < 2 years (112/402; 27.9%), and 2–5 years (36/402; 9%). A higher proportion of cases were males than females (65.6% versus 34.4%, respectively).

Of 421 patients with pneumococcal meningitis, 402 had positive CSF cultures for *S. pneumoniae* and 19 had negative cultures and positive latex agglutination results for *S. pneumoniae*. From 402 isolates, 397 were available for serotyping and antimicrobial susceptibility testing. These isolates represented 43 different serotypes. The predominant serotypes were 14 ($n = 55$; 13.9%), 3 ($n = 32$; 8.1%), 23F ($n = 32$; 8.1%), 19F ($n = 31$; 7.8%), 6B ($n = 30$; 7.6%), 18C ($n = 28$; 7.1%), and 6A ($n = 20$; 5%) (Table 2). We did not found any fluctuation in respect of yearly distribution of serotypes during the study period. The overall percentage of capsular types included in the 7-, 10-, and 13-valent vaccines accounted, respectively, for 50.9%, 51.9% and 67.3%.

Table 1
Incidence and case fatality ratio of pneumococcal meningitis cases detected in the population of the Metropolitan Region of Salvador during 2000–2007, according to different age groups.

Year	<1 year		<2 years		2-5 years		>5 years		Total	
	Incidence[a]	CFR[b] (%)	Incidence	CFR (%)	Incidence	CFR (%)	Incidence	CFR (%)	Incidence	CFR (%)
2000	27.9	35.7	13.7	35.7	3.3	0	0.6	6.3	1.12	17.1
2001	27.9	35.7	16.6	41.2	0.7	0	0.8	17.4	1.31	26.8
2002	17.9	55.5	8.8	55.5	1.3	0	0.5	28.6	0.80	36.0
2003	19.9	30.0	12.7	30.7	1.3	0	0.8	13.0	1.21	18.4
2004	8.0	50.0	6.8	28.6	2.0	100.0	0.5	14.3	0.76	37.5
2005	13.9	57.1	6.8	57.1	0.7	100.0	0.3	30.0	0.57	44.4
2006	18.0	25.0	6.8	14.3	2.0	66.6	0.7	31.6	0.92	31.0
2007	8.0	25.0	3.9	25.0	2.0	33.3	0.7	21.0	0.83	23.1

[a] Incidence per 100,000 population.
[b] Case Fatality Ratio.

For 382 patients of known age, the serotype coverage of the 7-, 10- and 13-valent pneumococcal conjugate vaccines (PCVs) is shown in Fig. 1. PCV-7 projected coverage was 69.9%, 74.7%, 74.3%, and 36.8% of *S. pneumoniae* isolates in patients <1 year, <2 years, 2–5 years, >5 years old, respectively. PCV-10 projected coverage was 72%, 77.4%, 74.3%, and 38% of isolates from patients in these age groups, respectively. The projected PCV-13 coverage was 79.6%, 82.8%, 82.9%, and 58.7% of *S. pneumoniae* isolates in patients <1 year, <2 years, 2–5 years, >5 years old, respectively. In children <5 years of age, PCV-7, PCV-10 and PCV-13 were projected to cover 74.3%, 75.7%, and 83.1% of the isolates, respectively. Non-vaccine serotypes were more common in patients >5 (41.3%) years of age, followed by patients 2–5 (34.2%) years and patients <1 (20.4%) year of age.

The antibiotic susceptibilities of the 397 *S. pneumoniae* isolates are summarized in Table 2. All isolates were susceptible to vancomycin and clindamycin, and ≥98% of isolates were susceptible to ofloxacin, cefotaxime, erythromycin, chloramphenicol (Clo), and rifampicin. Overall, 22.1% (n = 88) of isolates were non-susceptible to penicillin, 56% (n = 223) to trimethoprim–sulphamethoxazole (Sxt), and 29.6% (n = 117) to tetracycline. A total of 86.4% of PCV7 isolates were non-susceptible to penicillin, particularly among serotypes 14 (n = 37, 42%), 23F (n = 19, 21.6%), 6B (n = 10, 11.4%), and 19F (n = 9, 10.2%). Few penicillin-nonsusceptible pneumococci (PNSP) were found among other serotypes included in PCV10, PCV13 and among non-vaccine serotypes. Similarly, high percentages of nonsusceptibility to trimethoprim–sulphamethoxazole and tetracycline (tet) were

Table 2
Serotype distribution and antimicrobial non-susceptibilities of 397 S. pneumoniae isolates from patients with meningitis identified in Salvador, Brazil, during 2000–2007.

Serotype	No. (%) of isolates	Penicillin	Trimethoprim–sulphamethoxazole	Tetracycline	Ofloxacin	Cefotaxime	Erythromycin	Chloramphenicol	Rifampicin
All Serotypes	397 (100)	88 (22.2)	223 (56)	117 (29.6)	6 (1.5)	4 (1.0)	3 (0.8)	3 (0.8)	1 (0.3)
PCV7 serotypes									
All	203 (51.1)	76 (86.4)	134 (60.1)	46 (39.3)	3 (50)	4 (100)	1 (33.3)	1 (33.3)	0 (0)
14	55 (13.9)	37 (42)	47 (21.1)	13 (11.1)	2 (33.3)	4 (100)	1 (33.3)	0 (0)	0 (0)
6B	30 (7.6)	10 (11.4)	26 (11.7)	5 (4.3)	0 (0)	0 (0)	0 (0)	1 (33.3)	0 (0)
19F	31 (7.8)	9 (10.2)	24 (10.8)	3 (2,6)	1 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)
18C	28 (7.1)	0 (0)	9 (4)	3 (2.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
23F	32 (8.1)	19 (21.6)	20 (9.0)	18 (15.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
4	19 (4.8)	1 (1.1)	6 (2.7)	3 (2.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
9V	8 (2.0)	0 (0)	3 (1.3)	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
PCV10 serotypes									
All	208 (52.4)	76 (86.4)	136 (61)	47 (40.2)	3 (50)	4 (100)	1 (33.3)	1 (33.3)	0 (0)
+1	1 (0.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
+5	3 (0.8)	0 (0)	2 (0.9)	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
+7F	1 (0.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
PCV13 serotypes									
All	270 (68)	83 (94.3)	162 (72.6)	61 (51.7)	4 (66.7)	4 (100)	1 (33.3)	2 (66.7)	1 (100)
+3	32 (8.1)	0 (0)	4 (1.8)	6 (5.1)	0 (0)	0 (0)	0 (0)	1 (33.3)	0 (0)
+6A	20 (5.0)	3 (3.4)	15 (6.7)	5 (4.3)	1 (16.7)	0 (0)	0 (0)	0 (0)	1 (100)
+19A	10 (2.5)	4 (4.5)	7 (3.1)	3 (2.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Non-vaccine serotypes									
10A	13 (3.3)	0 (0)	5 (2.2)	12 (10.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
9N	10 (2.5)	0 (0)	5 (2.2)	8 (6.8)	2 (33.3)	0 (0)	1 (33.3)	1 (33.3)	0 (0)
6C	10 (2.5)	1 (1.1)	8 (3.6)	1 (0.9)	0 (0)	0 (0)	1 (33.3)	0 (0)	0 (0)
23B	9 (2.3)	2 (2.3)	7 (3.1)	2 (1.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
18A	9 (2.3)	0 (0)	1 (0.4)	5 (4.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
18F	8 (2.0)	0 (0)	3 (1.3)	3 (2.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
8	6 (1.5)	0 (0)	2 (0.9)	4 (3.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
11A	6 (1.5)	0 (0)	5 (2.2)	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
13	5 (1.3)	1 (1.1)	2 (0.9)	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
16F	6 (1.5)	0 (0)	4 (1.8)	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
15C	5 (1.3)	0 (0)	4 (1.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
NT	1 (0.25)	0 (0)	1 (0.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Others[a]	39 (9.8)	1 (1.1)	13 (5.8)	18 (15.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

[a] Including serotypes 7A (n = 1), 7B (n = 2), 7C (n = 1), 12F (n = 3), 15B (n = 3), 15F (n = 2), 17F (n = 4), 18B (n = 3), 20 (n = 4), 21 (n = 2), 22F (n = 1), 23A (n = 1), 28A (n = 1), 29 (n = 1), 34 (n = 4), 35B (n = 3), 35F (n = 1), 37 (n = 1), 39 (n = 1).

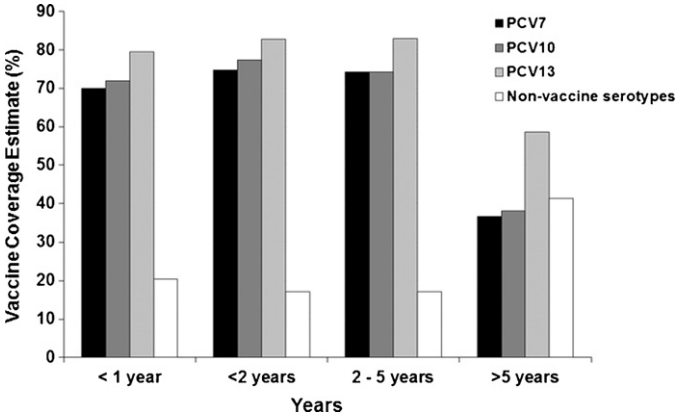

Fig. 1. Estimated projected coverage of the 7-, 10- and 13-valent pneumococcal conjugative vaccines (PCVs) for pneumococcal meningitis cases in Salvador, Brazil, during 2000–2007, according to different age groups.

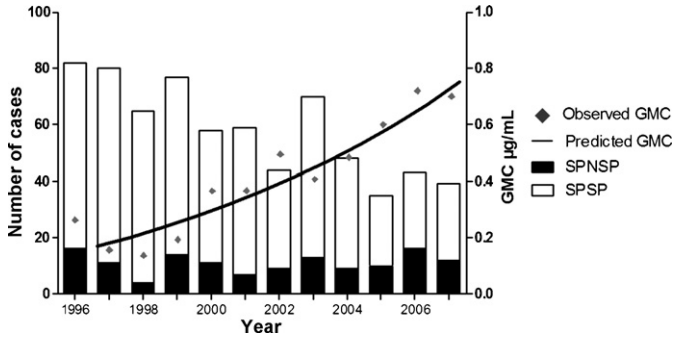

Fig. 2. Trends of geometric mean of penicillin MICs (μg/mL) over time and number of meningitis cases due to penicillin susceptible (SPSP) and non-susceptible (SPNSP) *S. pneumoniae* isolates, in Salvador, Brazil, 1996–2007.

found among PCV7 isolates. The most common serotypes showing nonsusceptibility to trimethoprim–sulphamethoxazole were serotypes 14 (n = 47, 21.1%), 6B (n = 26, 11.7%) and 19F (n = 24, 10.8%), whereas 15.4% of serotype 23F (n = 18) isolates and 11.1% of serotype 14 (n = 13) isolates were non-susceptible to tetracycline. Four (1%) serotype 14 isolates were cefotaxime non-susceptible (MIC = 1 μg/mL). This phenotype was associated with resistance to penicillin (MIC = 2 μg/mL; 2 isolates and MIC = 4 μg/mL; 2 isolates) (data not shown).

Overall, 295 (74.3%) of 397 *S. pneumoniae* isolates were non-susceptible to ≥1 drug. Resistance to ≥3 drugs (Sxt-Clo-Tet) was found in one serotype 6B isolate. All isolates of serotypes 23F, 5, 35B, 7B, 21, 7A, 7C, 22F, 23A, 29, 35F and 39, and ≥90% of isolates of the serotypes 6A (n = 18), 6B (n = 28), 9N (n = 10), 10A(n = 12), 19A (n = 9), and 14 (n = 51) were resistant to ≥1 drug (data not shown).

The trend of the geometric mean (GMC) of penicillin MICs during 1996–2007 is displayed in Fig. 2. Despite the decrease in meningitis cases due to penicillin-susceptible *S. pneumoniae* isolates (PSP), a significant increasing trend of GMC was found from 1996 to 2007 (P = 0.0001). After 2003, GMCs significantly increased to values as high as 0.25 μg/mL in 2006. Higher penicillin MICs were observed after 2001 (MIC = 2 μg/mL) and after 2004 (MIC = 4 μg/mL) among serotype 14 isolates (data not shown). The penicillin MIC_{50} and MIC_{90} found during the period of 2000–2007 were 0.031 μg/mL and 0.25 μg/mL, respectively.

4. Discussion

Our study describes the serotype distribution and antimicrobial susceptibilities of pneumococcal meningitis isolates collected in Salvador, Brazil during 2000–2007. These results represent an important contribution to our current understanding of the epidemiology and burden of pneumococcal meningitis prior to the introduction of PCV-10. The incidence of pneumococcal infection varies widely in different global regions and is influenced by several key factors such as age and immunization status [25]. Although we have detected a decline in the annual incidence of meningitis cases, in Metropolitan Salvador, from 2000 to 2007, the case-fatality ratio maintained high, particularly among children aged <5 years (41.9%). This finding may be related to the improvement of primary health care of patients and availability of 7-valent pneumococcal vaccine in private clinics since 2002. Otherwise, the maintenance of high rates of lethality may be related to intrinsic virulence properties of the pathogen and/or immunological conditions of the patients. It is important to point out that the active surveillance was maintained as the same during the period of study, without reduction in the number of sample-taking procedures. These evidences emphasize the need for continual IPD surveillance in our region

Fluctuations in the prevalence of individual serotypes may occur naturally in pneumococcal population in the absence of conjugate vaccine pressure [26]. However, we have observed through comparisons with our earlier surveillance data (29) that the distribution of the major serotypes among *S. pneumoniae* meningitis isolates has been stable over time in Salvador, with serotype 14 being the predominant serotype. The prevalence of the serotypes 14, 6B, 18C, 19F, and 23F causing meningitis reported by the Regional System of Vaccines (SIREVA), in Latin America, during 2000–2005 [27] also corroborates our surveillance results.

The predicted coverage of PCV7 (74.3%) and PCV10 (75.7%) within our study set of cases from children <5 years of age varied little, due to the low frequency of serotypes 1, 5, and 7F found among these meningitis isolates. However, in respect to PCV13, we observed an expanded covered of 83.1% in the same group of cases (children <5 years), related to the isolation of the serotypes 3 (n = 1; 0.7%); 6A (n = 6; 4.3%), and 19A (n = 3; 2.2%). The coverage percentages obtained here are in line with those expected for Latin America [27], and higher than those reported from other studies in Brazil, Bangladesh, and United States [28–30].

Since 1996 there has been an increase in penicillin nonsusceptibility of IPD isolates recovered in Salvador, Brazil. Between December 1995 and November 1999 15% of the *S. pneumoniae* meningitis isolates were penicillin non-susceptible (MICs, 0.125–1.0 μg/mL) [17]. The present study shows that the proportion of PNSP increased to 22.2% during 2000–2007. GMCs show an increasing trend over time, with values as high as 0.25 μg/mL in 2006, and penicillin-resistance was detected. In comparison with our previous study [17], penicillin MIC_{50} values increased from 0.016 μg/mL (1996–1999) to 0.031 μg/mL (2000–2007), while MIC_{90} maintained as the same value (0.25 μg/mL).

Most clinically significant antimicrobial resistance is confined to a small number of dominant, so-called "paediatric serotypes": 6A, 6B, 9V, 14, 19A, 19F and 23F [31]. Five of these serotypes are included in PCV10 (6B, 9V, 14, 19F and 23F) [32]. In the present study, 86.4% of PCV10 isolates were non-susceptible to penicillin, primarily including serotypes 14 (n = 37, 42%), 23F (n = 19, 21.6%), 6B (n = 10, 11.4%), and 19F (n = 9, 10.2%).

The high resistance rates found for trimethoprim/sulphamethoxazole (56%) and tetracycline (29.6%) are in agreement with the rates reported in other Brazilian studies [33,34]. This observation may be in part associated with antibiotic consumption [35], since these antimicrobial agents are among the most popular drugs, which are sold over the country without medical prescription and are usually administered improperly.

The identification of penicillin-resistant, cefotaxime-non-susceptible isolates, although few (n = 4; 1%) are of concern.

Cefotaxime has been the main antibiotic used for treatment of pneumococcal meningitis; however, in areas where beta lactam antibiotic-resistant pneumococcal strains are prevalent cefotaxime associated with vancomycin has been recommended as empirical treatment until susceptibility test results become available [36].

The findings in this report are subject to at least one limitation. The prevalence of serotypes detected during the period of study (2000–2007) and the estimated coverage of the conjugate vaccines are related only for *S. pneumoniae* isolated from meningitis cases. Information regarding other IPD manifestations in our region is often not available. In Brazil, meningitis is a compulsory reportable disease and the bacterial isolation from CSF is routinely performed. This is not the case for other IPD clinical specimens (for example blood or pleural fluid) where mandated diagnostic tests depend upon the physician's decision [30]. Although all of the pneumococcal isolates included in this study originated from only one hospital, this was not a limitation, since Hospital Couto Maia is the state reference hospital in the city of Salvador, with about 95% of the meningitis reports from the region originating from that site [15]

Serotype replacement with non-vaccine types after widespread use of PCVs remains a potential concern, requiring continual IPD surveillance to identify the emergence of new clinically important strains that can potentially acquire antibiotic resistance [37]. In the present pre-vaccine era we have observed that non-vaccine serotypes were most commonly recovered from patients 5–49 (42.4%) years and ≥50 (38.2%) years of age. In the coming years, results of continuous IPD surveillance will monitor the impact of the PCV10 implementation in Brazil. This information will be of great importance for healthcare decisions and further public health interventions that will potentially become necessary for further reducing the IPD burden in Brazil.

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