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Invasive Pneumococcal Disease Characterization in Adults and Subgroups aged < 60 years and ≥ 60 years in Bogota, Colombia

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ARTICLE INFO

Keywords:

Streptococcus pneumoniae, pneumococcal infection, adult, older adult, mortality healthcare resource utilization, antimicrobial resistance

ABSTRACT

Background: There is scarce information on the burden of invasive pneumococcal disease (IPD) among adults in low- and middle-income countries. This study aimed to describe the clinical outcomes and microbiological characteristics associated with IPD in adults and subgroups aged 18-59 years and ≥60 years in Colombia

Methods: A retrospective chart review study was conducted in five institutions of Bogotá from January 2011 to December 2017. Analyses were carried out for overall population and stratified by age group (18-59; ≥ 60 years)

Results: There were 169 IPD cases; median age was 58 years, 51.5% were male, and 80.5% had at least one comorbidity. Bacteremic pneumonia was the most common presentation (63.9%). The median length of hospital stay was 12 days with high healthcare resource utilization (HCRU): 58.6% required ICU and 53.3% inotropic support. Overall case-fatality rate (CFR) was 41.4%. Clinical outcomes were worse in patients ≥60 years old with significantly higher CFR and HCRU (ICU admission, mechanical ventilation, and inotropic support) compared to those aged 18-59 years. The most frequent serotypes were 3, 6 A/C, 14, and 19A. The sensitivity to penicillin in meningitis and non-meningitis isolates were 75% and 89.1% respectively

Conclusions: IPD was associated with a substantial burden in adults and worse clinical outcomes and HCRU in older adults in Colombia. Surveillance data combined with clinical outcomes have the potential to inform age-based pneumococcal vaccination policies.

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<https://doi.org/10.1016/j.ijregi.2022.04.007>

Received 22 February 2022; Received in revised form 18 April 2022; Accepted 22 April 2022

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Introduction

Pneumococcal infections are considered a public health problem, being associated with significant burden on healthcare systems and society (GBD Lower Respiratory Infections Collaborators, 2016). Younger children, older adults, and those with some underlying medical conditions are at higher risk of developing pneumococcal disease (CDC, 2015). Although *Streptococcus pneumoniae* colonization is mostly asymptomatic (Rodrigues et al., 2013; Trimble et al., 2020), the clinical spectrum of illness caused by these Gram-positive bacteria ranges from mild localized infections to more serious and life-threatening diseases requiring hospital admission to the intensive care unit (Rosselli and Rueda, 2012; Micek et al., 2020).

Fortunately, pneumococcal infections are vaccine-preventable diseases. Two types of pneumococcal vaccines are available: pneumococcal polysaccharide vaccine (PPSV) and pneumococcal conjugated vaccine (PCV). Each type is composed of the pneumococcal polysaccharide antigens that most frequently are associated with disease. The PPSV formulation contains the capsular polysaccharides of 23 serotypes (PPSV23), while PCV formulations contain a varying number of capsular serotypes conjugated to a nontoxic protein (e.g., PCV 10 and PCV 13) (CDC, 2015).

In Latin America, a region characterized by middle-income countries, PCVs were successfully introduced into the childhood national immunization programs (de Oliveira et al., 2016a; Agudelo et al., 2021; Parellada et al., 2021). In 2012, the PCV 10 was introduced into the Colombian National Immunization Program. It has since been available free of charge for all children with sustained high vaccination coverage rate (Ministerio de Salud y Protección Social, 2020). Except for Bogota, where PPSV23 vaccine is part of the publicly funded municipal immunization program for citizens aged ≥ 60 years, pneumococcal vaccine is not included in the national immunization schedule for older adults and populations at risk for pneumococcal disease in Colombia (Cano Gutierrez et al., 2016).

Despite a major decrease in the overall rate of pneumococcal disease in children (de Oliveira et al., 2016b; Shioda et al., 2020; Carrasquilla et al., 2021; Severiche-Bueno et al., 2021), a replacement of vaccine serotypes to non-vaccine serotypes has been observed after the introduction of PCV for children (Camacho Moreno et al., 2020; Agudelo et al., 2021). Unlike evidence available for children, indirect effects of childhood PCV vaccination on pneumococcal disease burden in adults are scarce in Latin America. Nevertheless, morbidity and mortality seem to remain high among adults (Whitney and Toscano, 2021; Severiche-Bueno et al., 2021).

Continued surveillance of invasive pneumococcal disease (IPD) is necessary to monitor serotype replacement, antimicrobial resistance, and vaccine impact among different age groups (Deloria et al., 2021). In Colombia, although bacterial meningitis is a notifiable disease, the surveillance of IPD is performed through a voluntary passive system. The isolates are collected from a national laboratory network and submitted to the National Institute of Health (*Instituto Nacional de Salud* [INS]) for confirmation, serotyping and antimicrobial susceptibility (Castañeda et al., 2009; INS, 2018; Severiche-Bueno et al., 2021). Moreover, a sentinel surveillance for bacterial pneumonia and meningitis in children under the age of five years was implemented in a tertiary pediatric hospital in Colombia (Camacho-Moreno et al., 2021). However, there is limited clinical characterization of IPD in adults in Colombia.

The aim of this study was to describe the clinical, epidemiological, and microbiological characteristics of hospitalized adults (18 to 59 years of age) and older adults (≥ 60 years of age) with IPD between January 1st, 2011 and December 31st, 2017 in five tertiary hospitals in Bogotá, Colombia. This study may contribute to a better understanding of morbidity and mortality associated with these infections in adults and the elderly, and how preventive strategies, such as vaccination, could reduce healthcare resource utilization (HCRU) and disease burden.

Materials and Methods

Study design and population

This was an observational, descriptive, and retrospective study in adults with a laboratory-confirmed diagnosis of IPD at five tertiary institutions in the city of Bogotá between January 1st, 2011 and December 31st, 2017. Patients aged ≥ 18 years with positive isolation for *S. pneumoniae* from sterile sites were identified from the clinical laboratory database at each institution participating in the study. Information on serotyping and antimicrobial susceptibility were obtained from INS, where isolates from these laboratories were submitted as part of an IPD passive surveillance (INS, 2018). Corresponding clinical information was collected through detailed chart review regarding patient demographics, vaccination history, underlying medical conditions, clinical presentation, case-fatality rate (CFR) and HCRU. Patients were excluded if medical history were not available.

Definitions

IPD was defined as an infection confirmed by the isolation of *S. pneumoniae* from a normally sterile body site. IPD clinical presentation was categorized as pneumonia, meningitis, bacteremia without focus and other. A community onset IPD was defined if patients presented associated IPD symptoms and diagnosis within the first 72 hours after admission and hospital onset IPD if symptoms had started after 72 hours. Adults were defined as population aged 18-59 years and older adults those aged ≥ 60 years. An underlying condition indicated a condition of interest or risk factor for pneumococcal disease described in the literature (CDC, 2015; Weycker et al., 2016) and contained in the patient medical record (e.g., chronic pulmonary diseases, chronic liver diseases, diabetes, smoking). The identified serotypes were categorized according to the available pneumococcal vaccines in Colombia as PCV 10 serotypes (1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F), PCV13 serotypes (comprising serotypes found in PCV10 plus serotypes 3, 6A, and 19A), PPSV 23 serotypes (comprising serotypes found in PCV 10 plus 2, 3, 8, 9N, 10A, 11A, 12F, 15B, 17F, 19A, 20, 22F, and 33F) and non-vaccine serotypes (not found in any vaccine, including non-typeable isolate).

Serotyping and antimicrobial susceptibility testing

Data on serotype, determined by Quellung reaction, were obtained through the INS surveillance system. The findings on antimicrobial susceptibility testing were obtained from the reports of the institutional laboratories or the microbiological laboratory of INS. Antimicrobial susceptibility to penicillin, ceftriaxone, and erythromycin was performed by broth micro-dilution method following 2017 Clinical and Laboratory Standards Institute procedure (Clinical and Laboratory Standards Institute, 2017).

Statistical analysis

A descriptive analysis was performed using central tendency and dispersion measures for continuous variables. For categorical variables, frequency distributions were obtained. Results were presented for the entire analysis population and stratified in two age groups: 18-59 years and ≥ 60 years. These age groups were chosen to better characterize IPD in adults and older adults. The analysis of serotype distribution was performed by individual serotypes and grouped by serotypes contained in different vaccines. Trends over time on serotype distribution and antimicrobial susceptibility were compared between early period post-childhood PCV 10 introduction (2011-2014) and late period (2015-2017).

Categorical variables were compared by chi-squared test or Fisher's exact test; for continuous variables, the Mann-Whitney U test was used. A p-value < 0.05 was considered statistically significant. The information

Table 1
Demographics and clinical characteristics in adults with invasive pneumococcal disease by age group in Bogotá, Colombia, 2011–2017

Characteristics	Age group (years)			p-value
	Totaln=169	18-59 yearsn=87	≥ 60 yearsn=82	
Participants (%)	169 (100)	87 (51.5)	82 (48.5)	
Age, median (IQR)	58 (45–70)	40 (30–43)	70 (65–78)	-
City of residence[‡]				
Capital (Bogota)	150 (88.8)	76 (87.4)	74 (90.2)	0.553
Another city	16 (9.5)	9 (10.3)	8 (9.7)	0.899
Sex				
Female	82 (48.5)	40 (48.8)	42 (51.2)	0.496
Male	87 (51.5)	47 (54)	40 (46)	0.496
Underlying medical conditions*				
Smoking	50 (29.6)	27 (31)	23 (28.0)	0.560
Alcoholism	27 (16.0)	16 (18.4)	11 (13.4)	0.369
Cardiovascular disease	56 (33.1)	15 (17.2)	41 (50.0)	0.000
Cancer	40 (23.7)	18 (20.7)	22 (26.8)	0.644
Chronic obstructive pulmonary disease	18 (10.7)	1(1.1)	17 (20.7)	0.000
Diabetes mellitus	28 (16.6)	7 (8.0)	21 (25.6)	0.006
Autoimmune disease	26 (15.4)	14 (16.1)	12 (14.6)	0.949
Previous episode of pneumonia	20 (11.8)	12 (13.8)	8 (9.8)	0.503
Antibiotic use in the last 3 months	24 (14.2)	14 (16.1)	10 (12.2)	0.762
HIV	11 (6.5)	11 (12.6)	0	0.004
Number of chronic medical diseases				
0	33 (19.5)	20 (23)	13 (15.9)	0.243
≥1	136 (80.5)	67 (77.0)	69 (84.1)	0.242
≥2	63 (37.3)	28 (32.2)	35 (42.7)	0.159
≥3	23 (13.6)	10 (0.6)	13 (0.8)	0.409

Values are given as n (%) unless otherwise noted.

* Patients could have more than one medical conditions

‡ Missing information for 3 patients (2 for 18–59 age group, and 1 for ≥ 60 years)IQR, interquartile range

was consolidated in Microsoft Excel® 13, and the statistical analysis was conducted in SPSS software.

The study was approved by the ethics committee of each one of the participating institutions: Hospital Universitario Clínica San Rafael, Fundación Hospital Infantil Universitario de San José, Hospital Universitario de San Ignacio, Fundación Neumológica Colombiana, and Subred Integrada de Servicios de Salud Centro Oriente ESE (Hospital Santa Clara).

Results

Demographic characteristics

During the seven-year study period, 177 hospitalized patients aged ≥18 years with laboratory confirmed IPD were identified. After excluding 8 patients without medical history, a total of 169 patients were included; 51.5% (n=87) were male, 48.5% (n=82) were ≥ 60 years old and 80.5% (n=136) had at least one comorbidity. Most patients resided in Bogota. The distribution by age group was 18–49: 29.6% (n=50), 50–59: 21.9% (n=37), 60–69: 22.5% (n=38), 70–79: 14.8% (n=25), and ≥ 80: 11.2% (n=19). Overall patient characteristics and stratified by age groups 18–59 years and ≥ 60 years are shown in [Table 1](#). Pneumococcal vaccine history was available for 18 (10.7%) cases: 16 were not vaccinated and two received PPSV 23.

Among patients aged ≥ 60 years, cardiovascular disease, diabetes mellitus, and chronic obstructive pulmonary disease were significantly more frequent compared to patients aged 18–59 years, while patients living with HIV were more frequent in those < 60 years ([Table 1](#)).

Clinical outcomes and healthcare resource utilization

The most common IPD clinical presentation was bacteremic pneumonia, followed by bacteremia without focus, and meningitis in overall population and in both age groups analyzed. A community onset IPD

Table 2

Clinical outcomes in hospitalized adults with invasive pneumococcal disease in Bogotá, Colombia, 2011–2017

Clinical presentation	Overall	18-59 years	≥ 60 years	p-value
Pneumonia	108 (63.9)	56 (64.4)	52 (63.4)	0.897
Bacteremia without focus	33(19.5)	15 (17.2)	18 (22.0)	0.440
Meningitis	23 (13.6)	12 (13.8)	11 (13.4)	0.942
Pneumonia and meningitis	1(100)	0	1(100)	
Other diagnosis*	4 (3.0)	4(4.6)	0	
Case-fatality rate				
Overall	70 (41.4)	25 (28.7)	44 (53.6)	0.000
Pneumonia	40 (37.0)	14 (25)	26 (50)	0.017
Bacteremia without focus	18 (54.5)	6 (40.0)	12 (66.7)	0.103
Meningitis	11 (47.8)	5 (41.7)	6 (54.5)	0.679
Pneumonia/meningitis	1(100)	0	1(100)	
Other diagnosis	1 (100%)	0 (0)	1 (100)	

Values are given as n (%) unless otherwise noted.

* 2 cases of primary peritonitis, 1 septic arthritis, 1 bacteremia with focus (cellulitis). One adult aged ≥ 60 y was diagnosed with pneumonia and meningitis, this case was excluded from the meningitis and pneumonia analysis.

was present in 89% (n=150) of the cases. Overall CFR was 41.4%, bacteremia without focus had the highest CFR (54.5%; n=18), followed by meningitis (47.8%; n=11) and pneumonia (37%; n=40). CFR was significantly higher in patients ≥60 years old (53.6%; n=44) compared with 18–59 age group (28.7%; n=25) in all clinical presentations. Bacteremia without focus had the highest CFR, followed by meningitis and pneumonia ([Table 2](#)).

An additional analysis of CFR by the most common serotypes (3, 14, 6A/C, and 19A) and age group is shown in [Table 3](#). Serotype 3 had the greatest CFR (46.2%), followed by 6C (42.9%), 19 A (30.0%), 6A (16.7%), and 14 (9.1%).

Overall median length of hospital stay was 12 days, 58.6% required ICU and 53.3% required inotropic support; the use of these resources was similar in both age groups. The ICU admission, mechanical ventila-

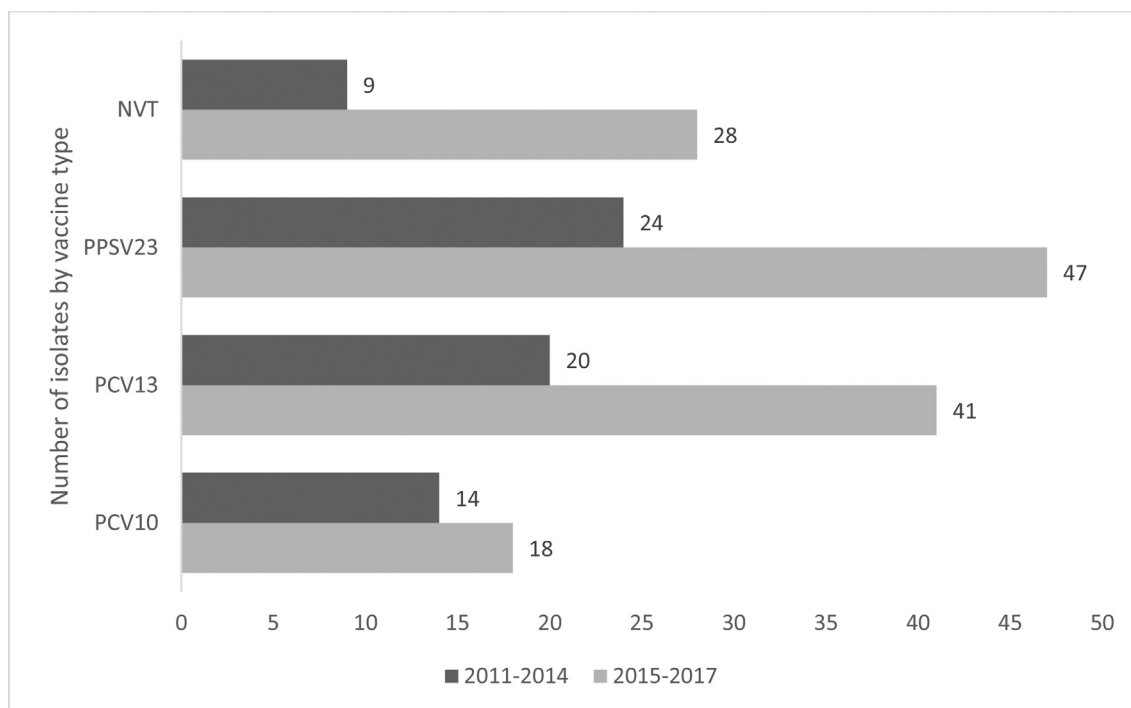


Figure 1. Serotype coverage by pneumococcal vaccine in adults with invasive pneumococcal disease, in the early and late period after PCV10 childhood introduction in Bogotá, Colombia, 2011-2017.

Table 3

Serotype-associated case-fatality rate in adults with invasive pneumococcal disease in Bogotá, Colombia, 2011-2017

Serotype	Case-fatality rate		
	Overall n/N (%)	18-59 years n/N (%)	≥ 60 years n/N (%)
3	6/13 (46.1%)	2/5 (40%)	4/8 (50%)
14	1/11 (9%)	0/8 (0%)	1/3 (33%)
19A	3/10 (30%)	2/6 (33%)	1/4 (25%)
6C	3/7 (42.8%)	0/3 (0%)	3/4 (75%)
6A	1/6 (16.6%)	1/4 (25%)	0/2 (0%)

CFR: case-fatality rate. Other serotypes were not included in this analysis due to the low numbers in the study sample

tion, and inotropic support in all IPD cases and by clinical presentation were significantly higher in the age group ≥ 60 years compared to those aged 18-59 years (Table 4; Supplementary material Appendix 1).

The initial antimicrobial treatment of IPD was empiric in 156 (92.3%) patients, and with a directed therapy in 8 (4.7%). A second and third regimen was administered to 125 (74%) and 79 (46.7%) patients after culture results or empirically based on clinical evolution. The median days (IQR) of antibiotic treatment for the first, second and third regimen were 4 (1-26), 4 (1-16), and 7.5 (1-24), respectively. The mean duration of antibiotic treatment was 12.9 ± 9.6 days.

Serotype distribution

Of 169 patients, 114 had serotyping data (67.5%). A total of 33 different serotypes were isolated and the main serotypes were 3, 14, 19A, 6C, and 6A during the study period (Table 5). No differences were seen in the most common serotypes among hospitalized patients with IPD by age group (Supplementary material Appendix 2).

From 2011-2017, the proportion of isolates from serotypes contained in PCV 10, PCV 13, PPSV 23 and non-vaccine serotypes were 28.1%,

50%, 62.3%, 32.5%, respectively (figure 1). A decrease in the proportion of the serotypes included in PCV 10 has been observed over the study period, with an increase in the proportion of serotypes not contained in the vaccines, mainly those included in PCV 13 (3, 6A, 19A) or in the PPSV 23 (3, 11A, 19A, and 22F). Comparing early (2011–2014) and late (2015–2017) periods after PCV 10 childhood introduction, a higher prevalence of serotype 3, 6A and 19A was found in the late period (8.8 to 12.5%, 2.9 to 6.3%, and 5.9 to 10%, respectively). Serotype 14 remained stable in both periods and serotypes 1 and 6B showed a marked reduction (11.8 to 0% and 8.8 to 1.3% respectively). Some serotypes not seen in the first period emerged in the second period: 15A (5%) and 35B (5%) (Table 5).

Antibiotic susceptibility

Over the study period, the susceptibility of meningitis isolates to penicillin was 75% and ceftriaxone was 77.2%. Regarding non-meningitis isolates, the susceptibility to penicillin, ceftriaxone, and erythromycin were 89.1%, 91.9%, and 85.3%, respectively. Among 19 isolates with decreased susceptibility to penicillin, 13 were serotyped (8 cases of serotype 14, 3 cases of 19F and one case of 15A and 35B). No increase in the antimicrobial resistance between early and late periods after PCV 10 childhood introduction was seen during the study period (Supplementary material Appendix 3).

Discussion

Although IPD is a public health problem of global interest, most pneumococcal epidemiology, serotype distribution, and disease burden data in adults are from high income countries in Europe and North America (Weycker et al., 2016; LeBlanc et al., 2017; Micek et al., 2020; Amin-Chowdhury et al., 2021; Isturiz et al., 2021). These findings could differ from low- and middle-income countries, and well-characterized data for adults is required (Deloria et al., 2021). This study corroborated with a recent study characterizing IPD in adults in Bogotá (Narváez et al., 2021), providing relevant additional information be-

Table 4
Healthcare resource utilization in adults with invasive pneumococcal disease by age group, in Bogotá, Colombia, 2011-2017

	Overalln=169	18-59 yearsn=87 (51.5)	≥ 60 yearsn=82 (48.5)	p value
Median LOS in days (IQR)	12 (4-20)	13 (6.5-23.5)	12 (3-19.8)	0.077
Required ICU, n(%)	99 (58.6)	47 (54)	52 (63.4)	0.216
LOS in ICU, days, median (IQR)	5 (2 – 13.3)	4 (2-10)	6 (2-14.3)	0.336
Required mechanical ventilation, n(%)	90 (53.3)	39 (44.8)	51 (62.2)	0.024
Median in days (IQR)	4 (1 – 12.8)	4 (1.5-12)	4 (1.5– 3.5)	0.042
Required inotropic drug support, n(%)	86 (50.9)	34 (39.1)	52 (63.4)	0.001
Median in days (IQR)	2 (1 – 4.8)	3 (1-5)	2 (1-4)	0.044

Values are given as n (%) unless otherwise noted.

ICU, intensive care unit; IQR, interquartile range; LOS, length of hospital stay

1 case ≥ 60 years was diagnosed with pneumonia/meningitis, it was excluded from the pneumonia and meningitis analyses.

Table 5
Changes in serotype distribution in adults with invasive pneumococcal disease, from early period to late period after PCV childhood introduction in Bogotá, Colombia, 2011-2017.

Pneumococcal serotypes	Overall period 2011-2017, n (%)	Period 2011-2017, n (%)	
		Early period (2011-2014) n = 34	Late period (2015-2017)n = 80
3	13 (11.4)	3 (8.8)	10 (12.5)
1	11 (9.6)	4 (11.8)	7 (8.8)
19A	10 (6.4)	2 (5.9)	8 (10.0)
6A	6 (5.3)	1 (2.9)	5 (6.3)
11A	4 (3.5)	1 (2.9)	3 (3.8)
6C	7 (6.1)	2 (5.9)	5 (6.3)
1	4 (3.5)	4 (11.8)	0 (0)
6B	4 (3.5)	3 (8.8)	1 (1.3)
15A	4 (3.5)	0 (0)	4 (5.0)
35B	4 (3.5)	0 (0)	4 (5.0)
PCV10	32 (28.1)	14 (41.2)	18 (22.5)
PCV13 no	29 (25.4)	6 (17.6)	23 (28.8)
PCV10			
PCV13	61 (53.5)	20 (58.8)	41(51.3%)
PPSV23	71 (62.3)	24 (70.6)	47 (58.8)
NVT	37 (32.5)	9 (26.5)	28 (35.0)

Data are presented as No. (%) unless otherwise specified.

NVT, non-vaccine serotypes

tween the main differences in clinical outcomes and HCRU in the 18-59 years and ≥60 age groups. These stratified data by age-group are fundamental to support cost-effectiveness studies and to inform at-risk populations and age-based pneumococcal vaccination policies (Husereau et al., 2013).

Pneumococcal diseases have been associated with a substantial morbidity and premature mortality in Colombian adults; in 2012 it was estimated that 63,463 disability-adjusted life years were lost because of IPD (Rosselli and Rueda, 2012). Colombia's population is becoming older, it is estimated that the older adult population size will double from 7 million currently to 15.3 million in 2025 (Economic Commission for Latin America and the Caribbean, 2019). Older adults are typically more susceptible to pneumococcal disease, due to immunosenescence, and have more severe clinical outcomes (Pawelec et al., 2018), placing a large burden on HCRU. Moreover, it can be a source of social vulnerability in low- and middle-income countries. A study showed that Colombian older adults were active contributors in the family expenses, 24% were responsible for all house expenses and 61% had one or more people who depend on their income (Villar et al., 2016). Thus, pneumococcal infection prevention strategies become increasingly important not only to protect lives but also to attenuate the socio-economic burden for society.

Consistent with the results of other studies, our study found that roughly half of hospitalized patients were younger than 60 years

(LeBlanc et al., 2017; Lopardo et al., 2018; Marrie et al., 2018; Isturiz et al., 2021). Interestingly, approximately 80% of IPD cases in adults aged 18-59 years in our study had ≥ 1 risk factor(s) for pneumococcal disease. Although the local Infectious Disease Medical Society (*Asociación Colombiana de Infectología*) guidelines recommend pneumococcal vaccination in older adults and in adults of any age who have risk factors for IPD (Gómez Muñoz et al., 2016), it is not part of the Colombian immunization program for older adults and population at risk, which limits access to vaccination. Other countries in Latin America had implemented publicly funded pneumococcal vaccine programs for both populations, but countries struggle to achieve good coverage rates (Zintgraff et al., 2020; Deloria et al., 2021; Parellada et al., 2021).

Like previous studies (Naucner et al., 2017; Brandileone et al., 2018), we found a reduction in vaccine serotypes causing IPD and a substantial increase in non-vaccine serotypes after childhood PCV introduction. Moreover, we observed the increase in number of serotypes causing IPD in adults from 20 in the early period to 29 types in the late period post-introduction, although roughly 40% were represented by five serotypes (3, 14, 19A, 6C, and 6A). As previously reported in other countries (Waight et al., 2015; Naucner et al., 2017; Brandileone et al., 2018), the serotype distribution in adults in Colombia largely reflected what has been observed in children under 5 years after the PCV implementation (Camacho Moreno et al., 2020). So, the most frequent serotypes found in the present study were similar to those observed in countries with PCV10 programs for childhood such as Brazil and Sweden (Naucner et al., 2017; Zintgraff et al., 2020). As expected, the serotype distribution causing IPD in Colombian adults differed from countries with PCV13 pediatric vaccination such as United States, England, and Argentina (Waight et al. 2015; Zintgraff et al., 2020; Isturiz et al., 2021).

In our study, overall CFR (41.4%) was remarkably high and even higher in older adults compared with those aged 18-59 years (53.6% vs. 28.7%). These findings contrasted with studies in Brazil (Dullius et al., 2018), Argentina (Ardito et al., 2016; Zintgraff et al., 2020), Belgium (Verhaegen et al., 2014), India (Jayaraman et al., 2019), and Japan (Fusukumi et al., 2017) that reported IPD CFR between 16% and 33%. The proportion of hospital-onset IPD in our study was similar to other studies that found it in 5-10% of the cases (Lyytikäinen et al., 2007; Kenig et al., 2019) and do not explain the higher CFR compared to other countries. Further studies are required to analyze other factors that can be contributing to increased CFR in Colombia. A higher CFR was observed for serotype 3 (46.2%) and 19A (30%), but it was difficult to draw definitive conclusions due to the lower number of other serotypes. Indeed, a higher proportion of complications and CFR with serotypes such as 14 and 6A have been reported in adults and older adults (Garcia-Vidal et al., 2010; Burgos et al., 2014).

The change in antimicrobial sensitivity of *S. pneumoniae* is a phenomenon that has become important in recent years in Colombia and other regions in the world. In our study, there was no increase in antimicrobial resistance over the study period. However, data from

the INS surveillance reported an increasing penicillin and ceftriaxone resistance to meningitis and non-meningitis isolates in the last years, mainly in serotypes 19A and 19F in older adults (INS, 2018; INS, 2019), consonant with findings in other Latin American PCV10 countries (Brandileone et al., 2021). This increased resistance in serotype 19A is associated with clonal complex CC320, as reported by Ramos et al., (2014), who found high rates of resistance to penicillin and ceftriaxone since 2012 in Colombia, and also has been documented in other PCV-10 countries (Brandileone et al., 2021). Also, multidrug resistance for serotype 6C associated with emergence of clonal complex CC386 has been reported in PCV-10 countries (Hjálmarsson et al., 2020; Brandileone et al., 2021). Besides the clonal expansion, the selective pressure exerted by the antimicrobial use has a significant role in the resistance pattern changes. All these elements reinforce the importance of continued antimicrobial surveillance for guiding antibiotic therapy policies.

The potential benefits of pneumococcal vaccines on the IPD burden in Colombian adults are dependent on the vaccine-preventable serotypes. The proportion of PCV 13 and PPSV 23 serotypes in the 2015–2017 period were 51.3% and 58.8%, respectively. Serotypes 3 and 19A have increased significantly in the last period in our study and data from 2019 Colombian surveillance showed an even greater proportion of serotype 19A (37%) and 3 (29%) in older adults (INS, 2019). Of note, serotype 6C (14%) was the third more frequent type in 2019, following the same trends of isolated serotypes in the pediatric population in Colombia (INS, 2019, Camacho Moreno et al., 2020). This emergence has been reported in other PCV-10 countries (Naucner et al., 2017; Brandileone et al., 2018), suggesting that PCV-10 does not induce cross-protection for 6C and consequently does not provide herd protection for this serotype in older populations.

This study has some limitations. First, the retrospective chart review design and IPD passive surveillance may have led to underreported data including the lack of information on vaccination status, pneumococcal serotyping, and antimicrobial resistance testing. Second, *S. pneumoniae* identification from the tertiary hospital's laboratories database may have caused selection bias toward more severe cases. Third, it should be considered that data were mainly from Bogota and the results might not necessarily be representative of the different regions of Colombia. Lastly, the numbers of cases in some analyses were too small to draw definitive conclusions.

Local studies are fundamental to characterize pneumococcal disease and to understand serotype distribution dynamics and its economic impact in adults. This study added valuable information to the literature detailing the main differences in clinical outcomes and HCRU between the 19–59 years and ≥ 60 age groups. Our findings reinforce the importance of surveillance data combined with clinical outcomes to inform vaccination policy for older adults and adult populations at risk for pneumococcal disease.

Conclusions

IPD was associated with a substantial burden of unfavorable outcomes, such as critical care need, high CFR, and resource overconsumption in adults and older adults in Colombia. Surveillance data combined with clinical outcomes have the potential to inform policy around adult pneumococcal vaccination.

Author contributions

Conception, design of work or acquisition: ALLC, GCM, CB, EP, MR, JR

Analysis and interpretation of data: ALLC, GCM, ANA, FVV, CA, SVB, BEA, OP, AYS, NSF, PR, CB, EP, JR, MR, JUR CIP

Drafting the manuscript and/or revising/reviewing the manuscript for important intellectual content: ALLC, GCM, ANA, FVV, CA, SVB, BEA, OP, AYS, NSF, PR, CB, EP, MR, JUR, CIP

All authors are responsible for the work described in this paper. All authors reviewed and approved the final version of the manuscript.

Funding

This work was supported by MSD Colombia, a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Acknowledgements

To all the participating institutions that supported the development of the study activities, to the Microbiology Laboratory of the National Institute of Health, and to the Asociación Colombiana de Infectología (ACIN capítulo central) as the executing institution of the project.

Disclosure of competing interest

CB, EP, MR, JR, JUR, and CIP are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ USA, who may own stock and/or hold stock options in Merck & Co., Inc., Kenilworth, NJ, USA. GCM and ALC received invitation to participate in scientific congresses from Pfizer, MSD and fees for taking part in advisory boards on vaccines from the same companies.

SVB is speaker for MSD, Pfizer, Biotoscana and Advisory boards from GSK, MSD, and Biotoscana. Other authors have no conflicts of interest. Asociación Colombiana de Infectología (ACIN capítulo central) was contracted to conduct this study

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.ijregi.2022.04.007](https://doi.org/10.1016/j.ijregi.2022.04.007).

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