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Are risk factors associated with invasive pneumococcal disease according to different serotypes?

Pilar Ciruela,[1,*] Núria Soldevila,[2] Laura Selva,[3] Sergi Hernández,[1] Juan Jose Garcia-Garcia,[4] Fernando Moraga,[5] Mariona F. de Sevilla,[4] Gemma Codina,[6] Ana Maria Planes,[6] Cristina Esteva,[3] Francis Coll,[5] Neus Cardeñosa,[2] Iolanda Jordan,[7] Joan Batalla,[1] Luis Salleras,[2,8] Carmen Muñoz-Almagro[3] and Angela Domínguez[2,8]

[1]Public Health Agency of Catalonia; Barcelona, Spain; [2]CIBER de Epidemiología y Salud Pública (CIBERESP); Madrid, Spain; [3]Molecular Microbiology Department; University Hospital Sant Joan de Déu; Esplugues de Llobregat, Spain; [4]Department of Pediatrics, University Hospital Sant Joan de Déu; Esplugues de Llobregat, Spain; [5]Department of Pediatrics; University Hospital Vall d' Hebron; Barcelona, Spain; [6]Microbiology Department; University Hospital Vall d' Hebron; Barcelona, Spain; [7]Pediatric ICU Department; University Hospital Sant Joan de Déu; Esplugues de LLobregat Spain; [8]Department of Public Health; University of Barcelona; Barcelona, Spain

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Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; ICU, intensive care unit; IPD, invasive pneumococcal disease; OR, odds ratio; PCR, polymerase chain reaction; PCV7, 7-valent pneumococcal conjugate vaccine; PCV10, 10-valent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; mo, month; y, year; d, day

The aim of this study was to investigate risk factors for the most common serotypes of invasive pneumococcal disease (IPD). A total of 293 IPD cases were analyzed in children aged 3–59 mo in a community with intermediate vaccination coverage with the 7-valent pneumococcal vaccine (PCV7). IPD cases were reviewed during 2007–2009 in two pediatric hospitals in Catalonia (Spain). A multivariate analysis using unconditional logistic regression was performed to estimate the adjusted odds ratio. PCV7 coverage was 45.4%. Pneumonia with empyema (64.5%) was the most frequent clinical manifestation. The most common serotypes were: serotype 1 (21.2%), 19A (16.0%), 3 (12.6%) and 7F/A (6.8%). 70.0% of serotypes found were included in the 13-valent conjugate vaccine (PCV13), 39.2% in the 10-valent conjugate vaccine and 8.1% in the PCV7. PCV7 was protective in IPD cases due to PCV7-serotypes (aOR: 0.15, 95% CI: 0.04–0.55). Serotype 1 was positively associated with attending day care or school (aOR: 3.55, 95% CI: 1.21–10.38) and age 24–59 mo (aOR: 7.70, 95% CI: 2.70–21.98). Serotype 19A was positively associated with respiratory infection in the previous month (aOR: 2.26, 95% CI: 1.03–4.94), non-penicillin susceptible IPD (aOR: 1.89, 95% CI: 1.13–3.16) and negatively associated with age 24–59 mo (aOR: 0.19, 95% CI: 0.09–0.41). Serotype 3 was positively associated with vaccination (aOR: 4.87, 95% CI: 2.05–11.59). No factors were associated with serotype 7F/A. Vaccination with pneumococcal vaccines including more serotypes may reduce the risk of disease in our setting.

Introduction

Invasive pneumococcal disease (IPD) is a serious public health problem caused by *Streptococcus pneumoniae.* The main component of virulence of the bacterium is the polysaccharide capsule, which facilitates cell invasion and development of the disease. Ninety-three serotypes have been described according to the polysaccharide proteins that constitute the capsule. Various host-related factors (age, genetic factors,[1] risk medical conditions[2]), environmental factors (day care attendance,[2,3] difficulty in accessing health services[2]) and geographical factors[4] may be associated with IPD.

The polysaccharide capsule is involved in many aspects of the epidemiology of IPD. An inverse relationship between carrying a given serotype and its invasiveness[5] and between the invasiveness and severity of the disease[6] has been postulated. Relationships between the serotype and age, clinical presentation,[7] disease evolution[8,9] and antibiotic resistance[10,11] have been reported.

After the introduction of the seven-valent pneumococcal conjugate vaccine (PCV7), associations have been maintained between IPD and some risk factors such as day care attendance but the association with other factors, such as breastfeeding, has disappeared.[2]

Although the PCV7 is not included in the official vaccination schedule in Catalonia, many pediatricians recommend it in clinical practice and parents pay for the vaccine. However, children aged < 5 y with risk factors receive the vaccine free of charge at 2, 4 and 6 mo, with a booster dose during the second year of life, according to the vaccination schedule contained in the summary

*Correspondence to: Pilar Ciruela; Email: pilar.ciruela@gencat.cat
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Table 1. General characteristics of cases included in the study and risk factors for IPD associated with PCV7 serotypes

	All cases (n = 293), %	PCV7 serotypes (n = 26), %	Non-PCV7 serotypes (n = 267), %	OR (95% CI)	aOR (95% CI) [a]
Sex-male	53.9	61.5	53.2	1.41 (0.62 – 3.22)	1.51 (0.59 – 3.84)
Age					
3–23 mo	39.2	61.5	37.1	Reference	Reference
24–59 mo	60.8	38.5	62.9	0.37 (0.16 – 0.84)	0.50 (0.18 – 1.38)
Vaccination status					
Non vaccinated	46.8	76.9	43.8	Reference	Reference
Vaccinated	45.4	19.2	47.9	0.23 (0.08 – 0.63)	0.15 (0.04 – 0.55)
Day care or school attendance	81.3	64.0	83.0	0.36 (0.15 – 0.88)	0.34 (0.13 – 0.89)
Antibiotic treatment	14.3	20.0	13.8	1.56 (0.55 – 4.43)	2.13 (0.66 – 6.82)
Respiratory infection	47.7	48.0	47.7	1.01 (0.44 – 2.30)	0.81 (0.30 – 2.22)
Breastfeeding	9.6	11.5	9.4	1.26 (0.35 – 4.50)	0.56 (0.13 – 2.40)
Exposure to tobacco in home					
0 cigarettes/d	59.6	52.2	60.3	Reference	Reference
1–19 cigarettes/d	19.3	30.4	18.3	1.92 (0.72 – 5.16)	3.16 (0.96 – 10.43)
≥ 20 cigarettes/d	21.1	17.4	21.4	0.94 (0.29 – 3.03)	1.10 (0.28 – 4.23)
Cohabitants > 4 persons	24.5	34.8	23.6	1.73 (0.70 – 4.28)	1.18 (0.43 – 3.25)
Siblings < 5 y	30.5	39.1	29.7	1.52 (0.63 – 3.66)	1.38 (0.54 – 3.53)
Social class					
I-III	59.6	34.8	62.0	Reference	Reference
IV-V	40.4	65.2	38.0	3.06 (1.25 – 7.51)	2.03 (0.78 – 5.31)
Risk medical conditions	1.4	3.8	1.1	3.52 (0.35 – 35.11)	8.16 (0.65 – 102.43)
ICU	14.0	23.1	13.1	1.99 (0.75 – 5.29)	1.45 (0.46 – 4.58)
Death	1.0	3.8	0.7	5.30 (0.46 – 60.52)	1.67 (0.11 – 25.87)
Non-penicillin susceptible[b]	34.8	70.6	28.6	2.45 (1.39 – 4.31)	2.01 (1.04 – 3.90)

Notes: [a]Adjusted for age, vaccination with ≥ 1 dose of PCV7, attending day care or school, antibiotics prescribed within 30 d before the onset of clinical symptoms and previous respiratory infection. [b]Antibiogram was performed in cases diagnosed by culture (n = 115). Abbreviations: y, year; m, months; d, days; OR, odds ratio; aOR, adjusted odds ratio; PCV7, 7-valent pneumococcal conjugate vaccine; ICU, intensive care unit; IPD, invasive pneumococcal disease.

of product characteristics.[12] Current estimated vaccination coverage is around 50%.[13]

The aim of this study was to investigate the association between the serotypes of *S. pneumoniae* most commonly found in our setting and risk factors for IPD after PCV7 licensing.

Results

Clinical characteristics. A total of 315 cases of IPD were diagnosed in children aged 3–59 mo. Twenty cases were excluded because the serotype could not be determined and two cases because the vaccination status could not be established. Of the 293 cases finally analyzed, 115 (39.2%) were diagnosed by culture and 178 (60.8%) by real-time PCR. The mean age was 30.2 mo (SD: 15.5). The clinical manifestations included pneumonia with empyema (64.5%), pneumonia without empyema (15.7%), meningitis (9.6%), non-focal bacteremia (7.5%), osteoarticular infection (1.7%), cellulitis (0.7%) and sepsis (0.3%).

The most frequent serotypes were: serotype 1 (62 cases, 21.2%), 19A (47 cases, 16.0%), 3 (37 cases, 12.6%) and 7F/A (20 cases, 6.8%). PCV7 serotypes represented only 8.9% (26 cases) of isolates. Serotypes included in the 10-valent pneumococcal conjugate vaccine (PCV10) represented 39.2% (115 cases) and serotypes included in the 13-valent pneumococcal conjugate vaccine (PCV13) represented 70% (205 cases).

Table 1 shows the risk factors analyzed in all study children: 45.4% (133/293) were fully vaccinated for their age, 14% (41/293) required ICU admission and 1% (3/293) died. Of the 115 cases diagnosed by culture, 34.8% (40 cases) were non-penicillin susceptible.

Associated factors according to serotype. Comparison of cases of IPD caused by PCV7 serotypes and non-PCV7 serotypes showed a positive association between IPD and non-penicillin susceptible strains (aOR: 2.01, 95% CI: 1.04–3.90) (**Table 1**) and non-focal bacteremia (aOR: 3.41, 95% CI: 1.02–11.35) (**Table 3**). PCV7 serotypes were negatively associated with PCV7 vaccination (aOR: 0.15, 95% CI: 0.04–0.55) and attendance at day care or school (aOR: 0.34, 95% CI: 0.13–0.89) (**Table 1**).

Analysis of the serotypes most frequently found in this study (serotype 1, 19A, 3 and 7F/A) showed a positive association

between IPD due to serotype 1 and the 24–59 mo age group (aOR: 7.70, 95% CI: 2.70–21.98) and attendance at day care or school (aOR: 3.55, 95% CI: 1.21–10.38) (**Table 2**). All cases presented pneumonia, of which 75.8% were with empyema (aOR: 2.57, 95% CI: 1.33–4.96) (**Table 3**).

IPD due to serotype 19A was positively associated with respiratory infection in the previous month (aOR: 2.26, 95% CI: 1.03–4.94), non-penicillin susceptible strains (aOR: 1.89, 95% CI: 1.13–3.16) (**Table 2**) and pneumonia with empyema (aOR: 7.80, 95% CI: 2.91–20.86) (**Table 3**) and negatively associated with the 24–59 mo age group (aOR: 0.19, 95% CI: 0.09–0.41) (**Table 2**) and pneumonia without empyema (aOR: 0.19, 95% CI: 0.05 to 0.66) (**Table 3**).

IPD due to serotype 3 was positively associated with vaccination (aOR: 4.87, 95% CI: 2.05–11.59) (**Table 2**) and pneumonia with empyema (aOR: 3.01, 95% CI: 1.22–7.43) (**Table 3**).

Serotype 7F/A was not associated with any of the factors studied.

Discussion

The results of this study show that age, PCV7 vaccination, attendance at day care or school, previous respiratory infection and non-susceptibility to penicillin were associated with IPD due to certain serotypes. Empyema was the clinical presentation most often associated with serotypes 1, 3 and 19A. The most frequent serotypes in our study were non PCV7 serotypes, namely serotypes 1, 19A, 3 and 7F/A, which represented 56.7% of cases. Serotypes 1, 19A, 3 and 7F are included in the 13-valent conjugate vaccine and serotypes 1 and 7F in the 10-valent vaccine.

IPD due to PCV7 serotypes had a higher risk of non-focal bacteremia and disease caused by non-penicillin susceptible strains, coinciding with other studies,[10,14] and were also more frequent in children aged < 24 mo. Non PCV7 serotypes were more frequent in children aged 24–59 mo, although the differences were not significant, probably due to the low number of cases. PCV7 serotypes were less frequent in vaccinated children, reflecting high PCV7 effectiveness[13,15] and in children attending day care or school, possibly because these children are more frequently vaccinated, due to pediatric advice.[16]

An increased incidence of pneumonia with empyema due to serotype 1 after the introduction of the PCV7 has been reported in some geographical areas.[17-19] In our setting, serotype 1 was the most common serotype and was associated with pneumonia with empyema. It was observed more frequently in children aged 24–59 mo and children attending day care or school. A possible explanation could be the presence of clone ST306 in serotype 1 strains in our setting.[20] This clone is susceptible to penicillin and may produce outbreaks in high density populations, and therefore close contact in day care facilities could facilitate the spread of the disease.[21] Day care attendance helps maintain the circulation of pneumococci in the population and increases carrier status[22,23] due to the greater number of people living in the environment and therefore may favor the development of microepidemics.[21]

After licensing of the PCV7, some regions saw an increase in IPD due to serotype 19A, making it the most frequent IPD-causing serotype.[24-27] In our study, serotype 19A was the second most common serotype after serotype 1. However, in contrast to serotype 1, serotype 19A was associated with age < 23 mo and disease due to non-penicillin susceptible strains, as reported by other authors.[7,18,27] Serotypes 3 and 19A were also associated with empyema, confirming the results of Byington et al.[19] after the licensing of the PCV7 in the United States. Previous respiratory infection, which has been described as a risk factor for IPD[28,29] was associated with serotype 19A. Tissue damage in respiratory tract cells caused by viral infections may explain this relationship. Serotype 19A is found in a large percentage of carriers, with different clonal expressions[11,27,30] and has a high capacity to produce IPD. This may be explained, at least in part, by an imbalance in host defense capacities, such as those caused by respiratory infections.[27,31]

Unlike serotypes 1 and 19 A, serotype 3 are found in a large percentage of carriers and has low invasiveness.[32] It has also been described as a serotype with high morbidity and mortality and greater involvement in adults.[33,34] In our study, serotype 3 was the third most common IPD-causing serotype, probably because molecular techniques allowed more cases to be diagnosed than in other studies.[20] Serotype 3 was more common in children aged 24–59 mo than in those aged < 24 mo, although the differences were not significant, possibly due to the small number of cases. Serotype 3 was associated with empyema. It was also associated with PCV7 vaccination and, although the finding must be confirmed in further studies, this association may be due to various factors. Bender et al.[35] found a high percentage of children with necrotizing pneumonia due to serotype 3 who had received any dose of PCV7 in relation to children with pneumonia due to other serotypes, although the differences were not significant. PCV7 exercises natural selection in the ecological niche of the nasopharynx and has been described as one of the factors responsible for the replacement of PCV7 serotypes by non-PCV7 serotypes.[7,36] Other reports have also observed an association between PCV7 vaccination and serotype 19A.[24,26] In our region, PCV7 coverage is intermediate and the results could differ in regions with higher coverages.

Serotype 7F has also emerged after the introduction of the PCV7. It has been reported to be a potentially invasive serotype[6] that acts as a primary pathogen, like serotype 1. In our study, serotype 7F/A serotype was the fourth most common serotype and was more frequent in cases with pneumonia than in other clinical presentations, although the differences were not significant, probably due to the low number of cases included. As reported by other studies[18] all strains were susceptible to penicillin.

The main strength of this study is the use of real-time PCR, which increased diagnostic sensitivity and enabled identification of a greater proportion of serotypes that are difficult to culture. Clinical data were collected from the medical history and sociodemographic data through a single survey of parents at the time hospitalization. Vaccination data were collected from the health records of each child (vaccination card or health card, medical history, hospital and primary care record). Therefore, it is unlikely that information bias may have invalidated our results.

Table 2. Risk factors for IPD according to serotype

	Serotype 1 (n = 62) %	Others (n = 231) %	aOR (95% CI)[a]	Serotype 19A (n = 47) %	Others (n = 246) %	aOR (95%CI)[a]	Serotype 3 (n = 37) %	Others (n = 256) %	aOR (95%CI)[a]	Serotype 7F (n = 20) %	Others (n = 273) %	aOR (95% CI)[a]
Sex-male	54.8	53.7	1.23 (0.65 – 2.34)	59.6	52.8	1.53 (0.73 – 3.22)	43.2	55.5	0.58 (0.28 – 1.21)	75.0	52.4	2.53 (0.88 – 7.28)
Age												
3–23 mo	8.1	47.6	Reference	70.2	33.3	Reference	43.2	38.7	Reference	50.0	38.5	Reference
24–59 mo	91.9	52.4	7.70 (2.70 – 21.98)	29.8	66.7	0.19 (0.09 – 0.41)	56.8	61.3	1.11 (0.45 – 2.73)	50.0	61.5	0.79 (0.27 – 2.34)
Vaccination status												
Non vaccinated	37.1	49.4	Reference	57.4	44.7	Reference	24.3	50.0	Reference	40.0	47.3	Reference
Vaccinated	53.2	43.3	1.14 (0.57 – 2.31)	40.4	46.3	0.61 (0.30 – 1.27)	73.0	41.4	4.87 (2.05 – 11.59)	55.0	44.7	1.69 (0.64 – 4.51)
Day care or school attendance	93.3	78.1	3.55 (1.21 – 10.38)	75.0	82.5	0.86 (0.35 – 2.12)	74.3	82.3	0.42 (0.17 – 1.01)	75.0	81.8	0.94 (0.26 – 3.27)
Antibiotic treatment	6.6	16.4	0.37 (0.12 – 1.16)	22.7	12.8	1.96 (0.76 – 5.03)	11.4	14.7	0.81 (0.24 – 2.75)	15.0	14.3	0.79 (0.20 – 3.12)
Respiratory infection	41.0	49.6	1.09 (0.46 – 2.90)	65.1	44.6	2.26 (1.03 – 4.94)	37.1	49.2	0.65 (0.29 – 1.48)	50.0	47.5	1.04 (0.38 – 2.85)
Breastfeeding	6.5	10.4	0.95 (0.28 – 3.14)	14.9	8.5	1.24 (0.41 – 3.69)	8.1	9.8	0.59 (0.14 – 2.43)	5.0	9.9	0.29 (0.03 – 2.50)
Exposure to tobacco in home												
0 cigarettes/d	63.3	58.6	Reference	72.1	57.4	Reference	62.9	59.2	Reference	52.6	60.8	Reference
1–19 cigarettes/d	13.3	10.3	1.30 (0.40 – 4.24)	16.3	19.8	0.70 (0.27 – 1.81)	17.1	19.6	0.83 (0.30 – 2.26)	26.3	18.8	1.73 (0.53 – 5.70)
≥ 20 cigarettes/d	23.3	20.5	0.77 (0.34 – 1.73)	11.6	22.8	0.41 (0.14 – 1.22)	20.0	21.2	1.04 (0.40 – 2.71)	21.1	21.1	1.29 (0.37 – 4.50)
Cohabitants > 4 persons	23.3	24.8	1.33 (0.59 – 3.01)	16.3	25.9	0.46 (0.18 – 1.20)	19.4	25.2	0.76 (0.28 – 2.07)	35.0	23.7	1.62 (0.57 – 4.62)

Notes: [a]Adjusted for age, vaccination with ≥ 1 dose of PCV7, attending day care or school, antibiotics prescribed within 30 d before the onset of clinical symptoms and previous respiratory infection. [b]Antibiogram was performed in cases diagnosed by culture (n = 115). Abbreviations: y, year; m, months; d, days; OR, odds ratio; aOR, adjusted odds ratio; IPD, invasive pneumococcal disease.

Table 2. Risk factors for IPD according to serotype (continued)

Siblings < 5 y	30.0	30.6	1.17 (0.58 – 2.35)	23.3	31.8	0.65 (0.28 – 1.52)	30.6	30.5	0.95 (0.42 – 2.15)	30.0	30.5	0.81 (0.29 – 2.25)
Social class												
I-III	69.6	56.9	Reference	56.1	60.3	Reference	63.6	59.0	Reference	52.6	60.2	Reference
IV-V	30.4	43.1	0.76 (0.36 – 1.57)	43.9	39.7	1.23 (0.56 – 2.71)	36.4	41.0	1.06 (0.47 – 2.39)	47.4	39.8	1.34 (0.50 – 3.55)
Intensive care unit	3.2	16.9	0.13 (0.02 – 1.03)	19.1	13.0	0.85 (0.34 – 2.12)	16.2	13.7	1.38 (0.50 – 3.82)	25.0	13.2	1.68 (0.50 – 5.65)
Non-penicillin susceptible[b]	0.0	46.0	—	60.0	25.9	1.89 (1.13 – 3.16)	16.7	35.8	0.71 (0.22 – 2.38)	0.0	38.1	—
Death	0.0	1.3	—	0.0	1.2	—	0.0	1.2	—	5.0	0.7	3.20 (0.20 – 51.19)
Risk medical conditions	0.0	1.7	—	0.0	1.6	—	0.0	1.6	—	0.0	1.5	—

Notes: [a]Adjusted for age, vaccination with ≥ 1 dose of PCV7, attending day care or school, antibiotics prescribed within 30 d before the onset of clinical symptoms and previous respiratory infection. [b]Antibiogram was performed in cases diagnosed by culture (n = 115). Abbreviations: y, year; m, months; d, days; OR, odds ratio; aOR, adjusted odds ratio; IPD, invasive pneumococcal disease.

A limitation of the study is the small number of cases produced by some serotypes, which made it difficult to obtain significant differences. Likewise, although adjustment was made in the multivariate analysis for all variables that might reasonably have affected the appearance of IPD, we cannot discard the possibility of some residual confounding.

Methods

Cases of IPD in children aged 3–59 mo attended by the Vall d'Hebron and the Sant Joan de Deu university hospitals between January 2007 and December 2009 were included.

The case definition of IPD was clinical signs of infection together with isolation in cultures from normally sterile sites or detection of *S. pneumoniae* DNA. Cases with no information on the vaccination status or without serotyping were excluded. Serotyping of strains isolated by culture was performed by Quellung reaction or Dot-blot at the Spanish National Microbiology Centre[37] and the study of serotypes in culture-negative cases was performed by real-time PCR at the Sant Joan de Deu university hospital.[20] Antibiotic sensitivity was evaluated using an agar dilution technique. Susceptibility to penicillin was defined according to the 2008 meningeal cut-off point criteria of the Clinical Laboratory Standards Institute.[38] Isolates with intermediate or resistant levels were defined as not susceptible.

Patient data were collected from medical records and by a questionnaire administered directly to parents or guardians at the time of diagnosis. The variables included in the study were: age, sex, clinical presentation, risk medical conditions, intensive care unit (ICU) admission, death, attendance at day care or school, previous antibiotic therapy, previous respiratory infection, breastfeeding, smoking exposure, number of inhabitants in the household, age of siblings and parental occupation. We also collected the serotype and antibiotic susceptibility of the microorganism.

The vaccination history was collected using health records (vaccination card or health card, medical history, hospital and primary care records). A child was considered vaccinated when they had received the full schedule for their age, having received the last dose (or only dose if this was the schedule corresponding to their age) of PCV7 ≥ 15 d before the onset of symptoms. Socioeconomic status was evaluated using the parental occupation according to the British classification.[39] We considered two levels: high (class I-III) and low (class IV-V). When there were discrepancies between the classification of the father and the mother, the highest classification was used. Information on antibiotic treatment, previous respiratory infection and breastfeeding was collected for the month before the onset of pneumococcal disease.

The crude association between the variable studied and being a case of IPD was assessed using the Chi-square test. A two-tailed distribution was assumed for all p-values. Multivariate analysis using unconditional logistic regression was used to estimate the adjusted odds ratio (aOR), including independent variables associated with both the risk factor and IPD, with a cut-off point of $p < 0.2$. The variables age, vaccination, attendance at day care or school, previous respiratory infection and previous antibiotic

Table 3. Association between clinical presentation and IPD caused by different serotypes

Clinical presentation	PCV7 Serotypes (n = 26), %	aOR (95% CI)[a]	Serotype 1 (n = 62), %[a]	aOR (95%CI)[a]	Serotype 19A (n = 47), %	aOR (95%CI)[a]	Serotype 3 (n = 37), %	aOR (95%CI)[a]	Serotype 7F (n = 20), %	aOR (95% CI)[a]
Pneumonia[b]	50.0	0.25 (0.08–0.79)	100.0	—	68.1	0.53 (0.25–1.13)	97.3	14.77 (1.79–121.70)	60.0	0.31 (0.09–1.07)
Empyema	19.2	0.28 (0.09–0.87)	75.8	2.57 (1.33–4.96)	57.4	7.80 (2.91–20.86)	75.7	3.01 (1.22–7.43)	35.0	0.45 (0.16–1.25)
Without empyema	30.8	1.18 (0.44–3.21)[1]	24.2	0.85 (0.41–1.76)	10.6	0.19 (0.05–0.66)	21.6	0.86 (0.36–2.04)	25.0	1.02 (0.35–2.96)
Meningitis	23.1	2.40 (0.72–7.94)[2]	0	—	12.8	0.41 (0.14–1.21)	2.7	0.22 (0.03–1.82)	20.0	2.08 (0.56–7.70)
Non-focal bacteremia	26.9	3.41 (1.02–11.35)	0	—	12.8	0.75 (0.24–2.37)	0.0	—	15.0	2.18 (0.52–9.06)
Others	0.0	—	0.0	—	6.4	1.10 (0.24–5.11)	0.0	—	5.0	1.35 (0.15–12.43)

Notes: [a]Adjusted for age, vaccination with ≥ 1 dose of PCV7, attending day care or school, antibiotics prescribed within 30 d before the onset of clinical symptoms and previous respiratory infection. [b]With and without empyema.

treatment were also included in the multivariate analysis. The analysis was performed using SPSS v18 (SPSS Inc. USA).

In all cases informed oral consent was obtained from parents or guardians, as participation in the study resulted in no further intervention other than the medical attention required by each patient. All information collected was treated in confidence as established by Spanish legislation on observational studies. The Institute of Health Studies of the Generalitat of Catalonia and the Ethics Committee of the Foundation of the Hospital Sant Joan de Deu approved the study.

Conclusions

Associations were found between some risk factors and IPD caused by specific serotypes. IPD due to PCV7 serotypes was less frequent in cases vaccinated with PCV7 and was associated with disease caused by non-penicillin susceptible strains and non-focal bacteremia. Risk factors for serotype 1 were attending day care or school and age 24–59 mo. Risk factors for serotype 19A were age < 24 mo, previous respiratory infection and disease due to non-penicillin susceptible strains. PCV7 vaccination was a risk factor for serotype 3, although other, unstudied factors might have influenced this association. Serotypes 1, 3 and 19A were associated with empyema. Vaccination with vaccines including more serotypes could reduce the risk of IPD in our setting.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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