

Clonal analysis of invasive pneumococci and its relationship with age group and antimicrobial susceptibility. Results of a multicenter study in Spain (2010-2014).

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INTRODUCTION and AIM

Streptococcus pneumoniae is a major cause of morbidity and mortality worldwide, being responsible for a wide variety of invasive diseases: bacteremic pneumonia, septicemia and meningitis. Children are the main reservoir for pneumococci and they represent the source of spread to adults, especially to the elderly. In the last years, new emerging serotypes have been detected in many countries mainly associated with the expansion of previously described clones or with the emergence of new clones.

The aim of this study was to analyze the clonal composition of *Streptococcus pneumoniae* isolates collected from young and older adults with invasive pneumococcal disease (IPD) in 9 Spanish hospitals.

METHODS

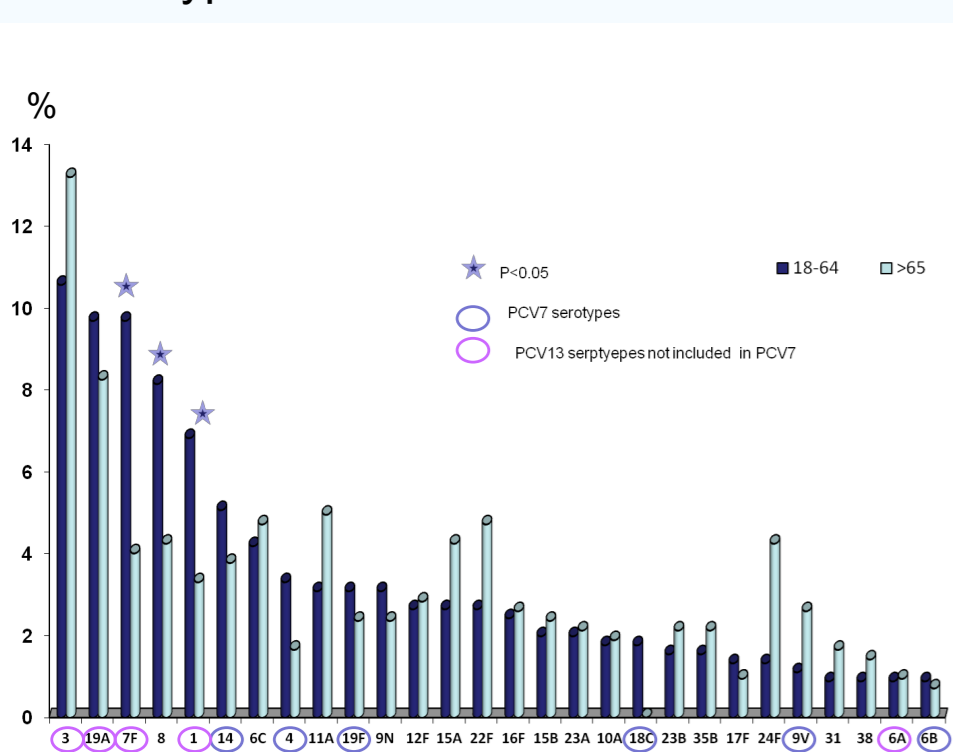
The study: Prospective, active, hospital-based surveillance of all culture-confirmed IPDs in adults (≥18 years) in 9 Spanish hospitals from August 2010 to May 2014. IPD was considered isolation of *S. pneumoniae* in normally sterile fluids (blood, cerebrospinal fluid, pleural fluid...).

Serotyping was performed by the Quellung reaction, dot blot assay or real-time PCR.

Molecular typing. The molecular typing was performed by pulsed-field gel electrophoresis (PFGE). Genomic DNA embedded in agarose plugs was restricted with SmaI or ApaI and fragments were separated by PFGE in a CHEF-DRIII apparatus. PFGE patterns were compared to representative international pneumococcal clones of the Pneumococcal Molecular Epidemiology Network (PMEN). (McGee L *et al.* J Clin Microbiol 2001;39:2565-71). In order to assess the identity with global pneumococcal clones, 84 isolates representative strain of major PFGE pattern (those that included > 4 isolates) were analyzed by MLST. The allele's number and sequence types (ST) were assigned using the pneumococcal MLST web site. (Enright MC. Microbiology 1998; 144:3049-60).

RESULTS

Serotype distribution of invasive isolates

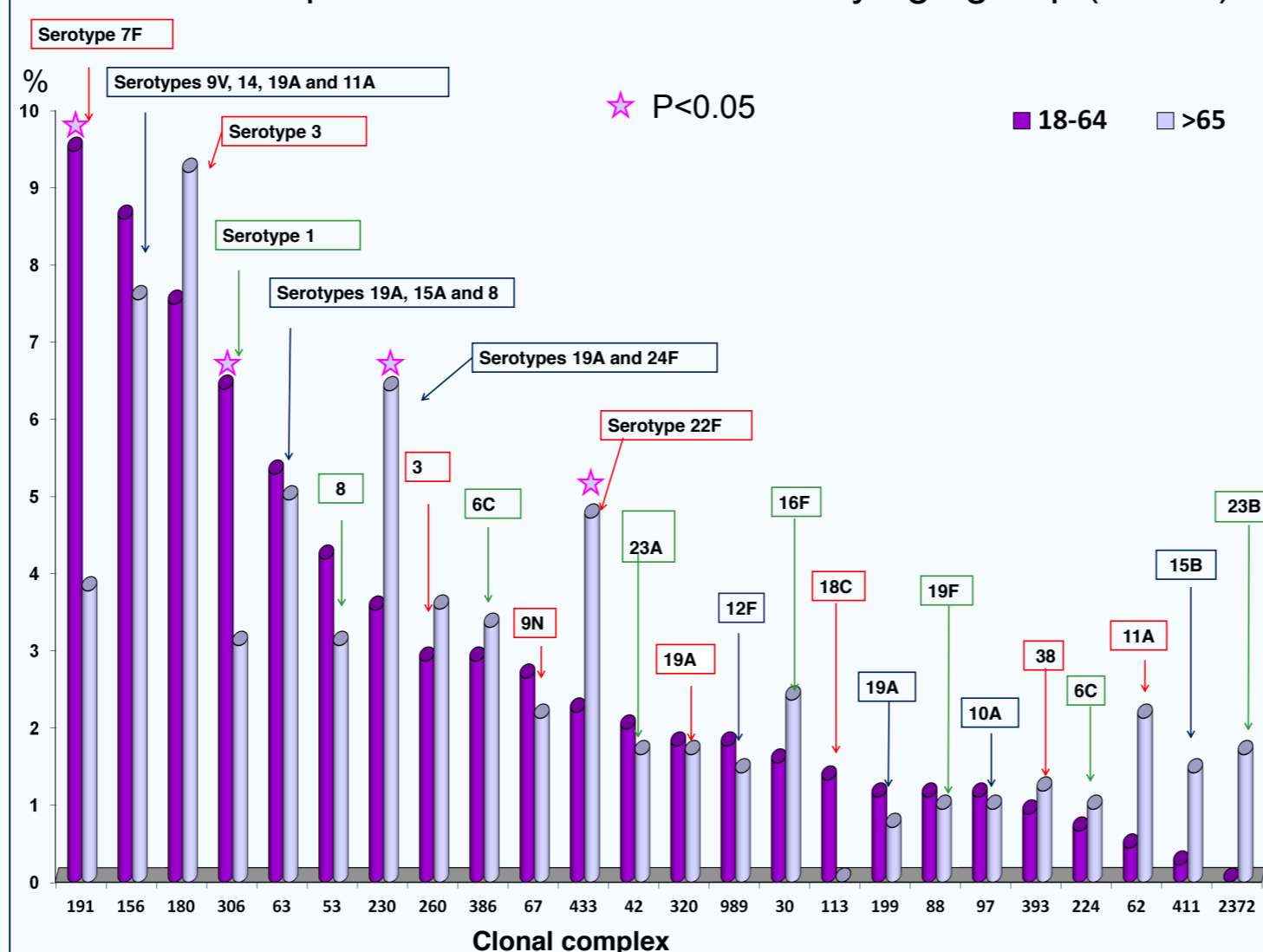


•A total of 878 cases of IDP were included during the study period. Of them, 454 were collected from young adults (18-64 years) and 424 were collected from older adults (>64 years).

• The most frequent serotypes among young and older adults were: 3 (10.6%, vs 13.2%, p=0.2), 19A (9.7% vs 8.3%, p=0.45), 7F (9.7% vs 4.0%, p=0.001), 8 (8.1% vs 4.2%, P=0.02), 1 (6.8% vs 3.3, p=0.018), 14 (5.1% vs 3.8, P=0.35), 6C (4.2% vs 4.7, P=0.7), 22F (2.6% vs 4.7%, P=0.1), 24F (1.3% vs 4.2%, P=0.08), 11A (3.1% vs 5.0%, P=0.16).

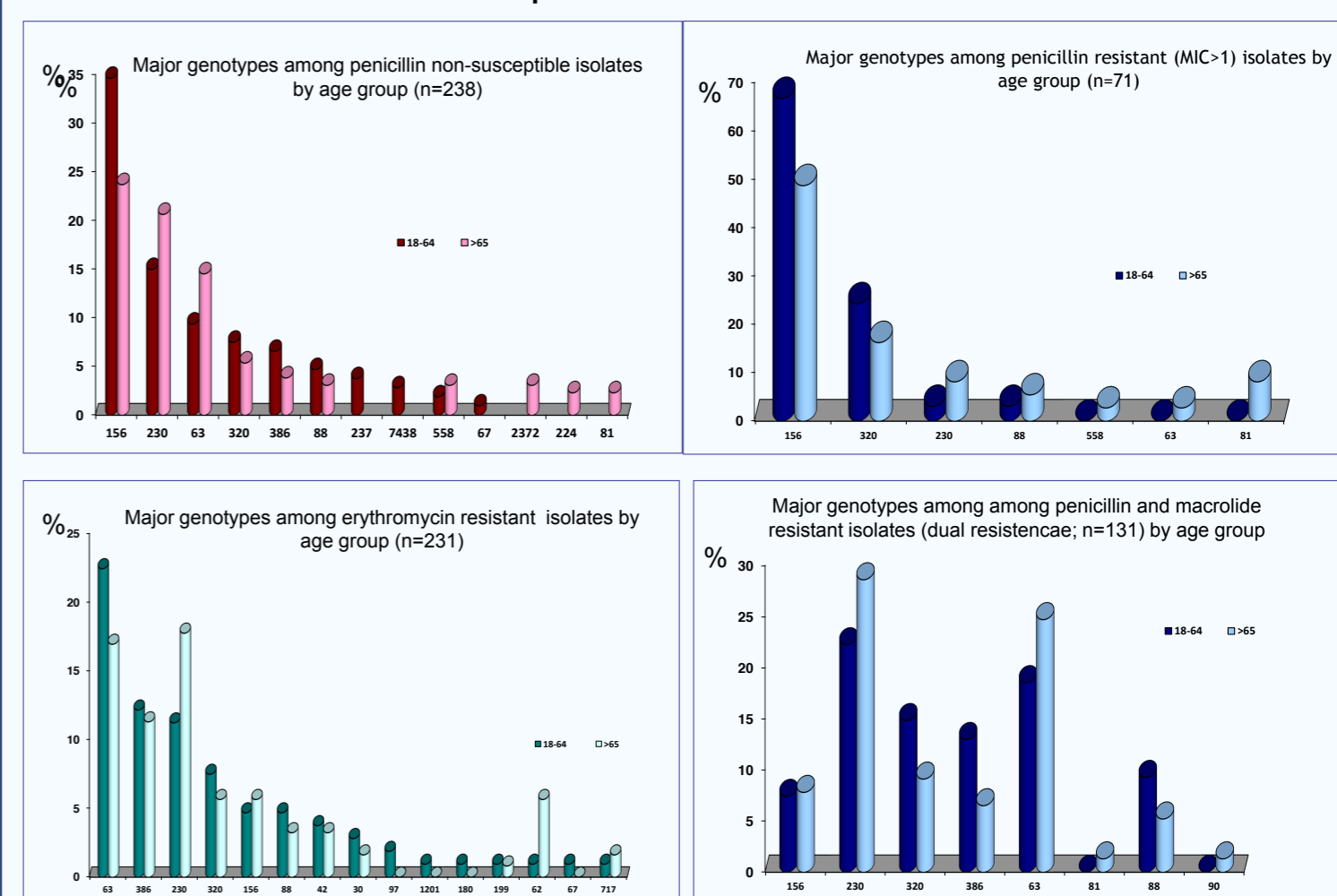
•The proportion of isolates included in the PCV13 were 53.1% for young adults and 42.7% for older adults (p=0.02).

Clonal composition of invasive isolates by age group (n=878)



The most frequent genotypes among young and older adults were: CC191 (9.5% vs 3.8%, serotype 7F, P=0.001), ST156 (8.6% vs 7.5%, serotype 14, 9V, 11A, 19A; P=0.6), CC180 (7.5% vs 9.2%, serotypes 3, P=0.36), ST306 (6.4%, vs 3.1% serotype 1, P=0.04), CC230 (.5% vs 6.4%, serotypes 24F and 19A, P=0.05), CC63 (5.3% vs 5.0%, P=0.8), and CC433 (2.2% vs 4.7%, P=0.04).

Clonal composition of resistant isolates



- PEN-R and ERY-R rates were lower among young than among older adults (23.6% vs 30.9%, p=0.015) and (23.6% vs 29.2%, p=0.06), respectively.
- PEN-R was associated with CC156 (28.6%, Stys 14, 9V, 11A and 19A), CC230 (18.1%, Stys 24F and 19A), CC63 (12.2%, serotypes 15A and 19F), CC320 (6.3%, serotype 19A) and CC386 (5.0%, serotype 6C).
- CC156 was most frequent among PEN-R isolates collected from young adults (34.6% vs 23.7%, p=0.06).
- These five clones were also the most frequent among ERY-R isolates and also among dual resistant isolates accounting for 76.4% of them.
- More than a half (57.1%) of high-level penicillin-resistant isolates (MIC >= 2mg/L) belonged to CC156 (serotypes 14, 9V, 19A and 11A), and 20% to CC320 (serotype 19A).
- Levofloxacin non-susceptibility (3.0%) was mainly associated with CC63 (65.4%, serotypes 8 and 15A) and CC156 (11.5%; serotype 9V)

CONCLUSIONS

- Invasive pneumococci collected from young adults showed lower resistance rates than those isolated from older people.
- These differences were associated with the clonal composition of invasive pneumococci in each age group.
- The major genotypes involved in penicillin- and erythromycin-resistance were CC156, CC230 and CC63.
- Three multidrug-resistant clones (CC230, CC63, and CC156) exhibited different capsular types included and non-included in the PCVs.

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