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Serotype Distribution and Antimicrobial Resistance of Invasive Pneumococcal Disease Strains in the Comunidad Valenciana, Spain, during the Winter of 2009-2010: Low PCV7 Coverage and High Levofloxacin Resistance

Streptococcus pneumoniae can cause serious invasive pneumococcal diseases (IPD), such as pneumonia, sepsis, and meningitis, and is the cause of major morbidity and mortality worldwide. The bacterium produces a capsule, of which over 90 serotypes exist and which forms the basis of the current conjugate vaccines (5). Since the introduction of the pneumococcal conjugate vaccine (PCV7) that protects against 7 serotypes (4, 6B, 9V, 14, 18C, 19F, and 23F), a shift in IPD-causing serotypes toward nonvaccine serotypes has been observed worldwide (2, 4, 10). Furthermore, after the initial decline since the introduction of PCV7, resistance against penicillin and macrolides in IPD-causing strains is on the rise again. Moreover, the novel occurrence of fluoroquinolone resistance has been reported, especially in these non-PCV7 serotypes (1, 7, 9). The first objective of this study was to determine the serotype distribution of IPD-causing *S. pneumoniae* strains in the

Published ahead of print 2 July 2012
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doi:10.1128/AAC.01201-12

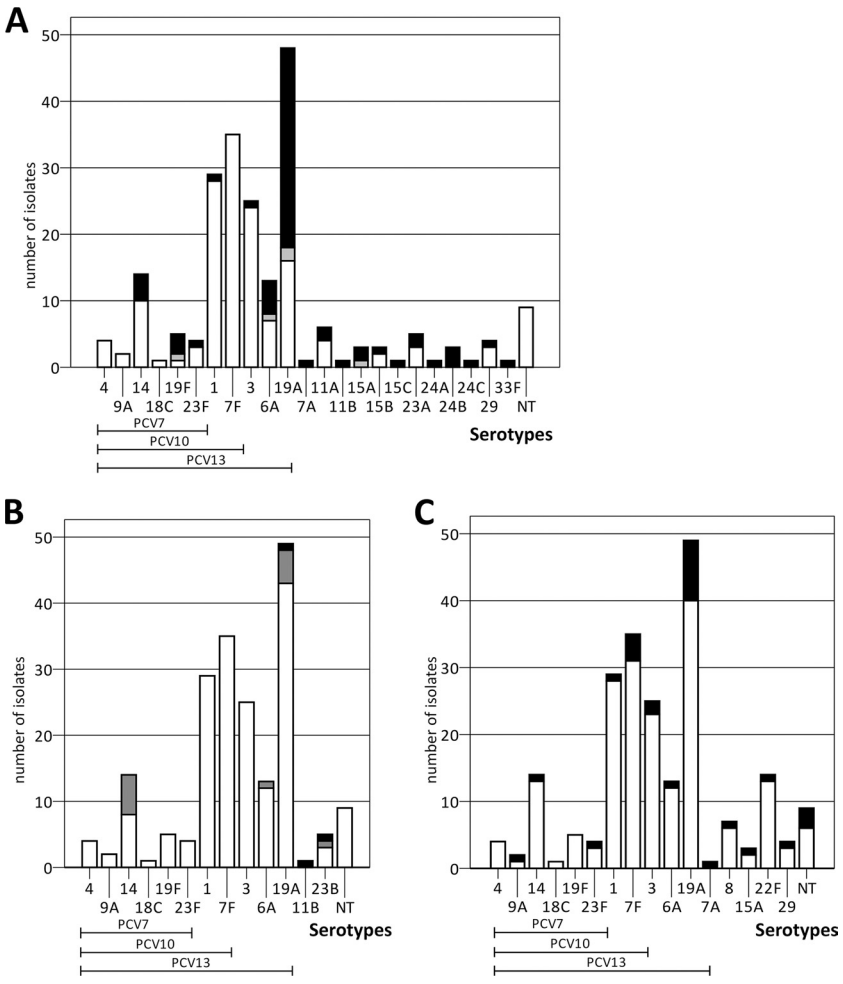

FIG 1 (A) Erythromycin, (B) penicillin, and (C) levofloxacin susceptibility organized by serotype. Only vaccine serotypes and serotypes with at least one nonsusceptible strain are shown. Resistance to all three antibiotics was mostly seen in serotype 19A. Furthermore, erythromycin resistance was predominantly seen in serotypes 6A, 14, 19F, and 24B, penicillin intermediate resistance was predominately seen in serotype 4, and levofloxacin resistance was frequently seen in serotype 7F. White, susceptible; gray, intermediate resistant; black, resistant.

Comunidad Valenciana, Spain, and the coverage rates of two new-generation conjugate vaccines, PCV10 (all PCV7 serotypes plus 1, 5, and 7F) and PCV13 (all PCV7 serotypes plus 1, 3, 5, 6A, 7F, and 19A). The second objective was to measure the antimicrobial resistance of these strains.

From September 2009 to March 2010, 285 IPD-causing *S. pneumoniae* strains were collected in the 22 participating hospitals in the Comunidad Valenciana and sent to the University Hospital La Fe. Serotyping was performed by serum slide agglutination (Denka Seiken, Tokyo, Japan). Antimicrobial resistance was determined using the Etest (AB Biodisk, Sweden). All 285 strains were tested for penicillin, amoxicillin-clavulanic acid, erythromycin, and levofloxacin susceptibilities, and 202 were tested for clindamycin, vancomycin, moxifloxacin, teicoplanin, linezolid, and tigecycline susceptibilities.

The most common serotypes were 19A (17.9%), 7F (13%), 1 (12.3%), and 3 (9.1%). Remarkably, only 11.7% of the IPD-causing strains had a serotype included in PCV7, whereas PCV10 covered 37% and PCV13 68.8% of all serotypes. In comparison to the serotype distribution in 2008 in the Comunidad Valenciana, the prevalence of 19A and 6A has risen from 14.9% to 17.9% and from 0.9% to 4.6%, respectively, increasing the coverage rate of PCV13 (3). Of the strains tested, 25% were erythromycin resistant (Fig. 1). Using the 2008 CLSI penicillin breakpoints, the majority of strains (94%) was susceptible, as opposed to 69% using the previous breakpoints. Strikingly, 10.6% of the strains were resistant to levofloxacin, in contrast to only 2% in 2008, a percentage that has never been observed in Spain before and is rare in other countries (6, 8, 9). Resistance against penicillin, erythromycin, and levofloxacin was predominantly seen in serotype 19A. Twenty-two strains (7.5%) were resistant to more than one class of antibiotic, the majority also being serotype 19A. This is in accordance with worldwide reports of high antimicrobial resistance in serotype 19A strains (2). In conclusion, PCV13 would be a valuable option for the vaccination calendars in the Comunidad Valenciana, not only for the prevention of invasive disease but also to stem the rise of levofloxacin and/or multiresistant serotype 19A strains. Furthermore, levofloxacin resistance in Valencia and in the rest of Spain is worrisome and should be closely monitored to prevent future treatment failure.

ACKNOWLEDGMENTS

We thank the Denka Seiken Company for generously providing the factor antisera used in this study, and we thank all technicians, microbiologists, and epidemiologist of the RedMiva of Comunidad Valenciana.

Parts of this work were made possible by a travel grant from the Junior Scientific Masterclass (University of Groningen, University Medical Center Groningen) to C.M.G. J.J.E.B. is a Rosalind Franklin Fellow of the UMCG.

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