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2) Early impact of 13-valent pneumococcal conjugate vaccine introduction to National Vaccination Program in children under 6 years old with invasive pneumococcal disease in Argentina

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Diseases caused by *S.pneumoniae* are a major worldwide public health problem especially in children. Since 1993 the *S. pneumoniae* Surveillance Program (SIREVA II-OPS/WHO) is conducted at the National Reference Laboratory (NRL). Thirteen-valent pneumococcal conjugate vaccine (PCV13) was introduced into Argentine National Vaccination Program in January 2012 for children <1 year old with 2 + 1 schedule and catch-up between 12-24 months. The aim was to evaluate changes in the serotype distribution and antimicrobial susceptibility among *S.pneumoniae* causing invasive disease (IPD) in children <6 years old before (pre-PCV13) and after (post-PCV13) the introduction of PCV13 in the National Schedule.

Methodology: *S.pneumoniae* isolates from 115 hospitals (21 provinces and Buenos Aires city) were received between January 2010 and December 2013 at the NRL. Isolates from sterile fluids were serotyped by Quellung reaction and MIC was performed by agar dilution (CLSI 2013). Three periods were defined: pre-PCV13 (2010-11), transitional (2012) and post-PCV13 (2013). Comparisons were established between pre-PCV13 and post-PCV13 period. $p < 0.05$ was considered statistically significant.

Results: From 1303 *S.pneumoniae* isolated in children <6 years old, 934 (71.7%) were <2 years old. Diagnosis: pneumonia (52.4%), meningitis (19.5%), sepsis (12.2%), other (15.9%). The number of cases of IPD received at the NRL decreased from 385 (annual average) in pre-PCV13 to 226 in post-PCV13. The serotype distribution (% pre-PCV13/%post-PCV13) was: 14 (22.3/7.1), 1 (13.5/17.1), 5 (12.6/6.6), 7F (5.8/6.2), 19A (5.8/3.5), 6A (5.7/1.8), 3 (3.4/7.1), 6B (5.1/2.7), NT (1.6/11.9), 18C (3.5/0.4), 23F (3/0.9), 12F (2.1/3.1), 9V (2.6/2.2), 19F (2.7/0.9), 4 (1.2/0.4) and others (11.9/28.5). We observed significant decrease in serotype 14, 5, 6A and 18C; and increase in NT and others. The prevalence of PCV13 serotypes decreased from 87.3% in pre-PCV13 to 57.5% in post-PCV13 ($p < 0.001$). Analyzing the prevalence of 13 serotypes included in PCV13, in both periods (pre/post-PCV13) by group of age we observed a coverage of 85.2%/49.7% in children <2 years old ($p < 0.001$) and 87.6%/73.3% in children of 3-5 years old ($p = 0.4$). Antibiotic resistance in pre-PCV13 and post-PV13 periods was: penicillin MIC ≥ 0.12 mg/L 35%/30%; penicillin MIC ≥ 4 mg/L 0.3%/0%; cefotaxime MIC ≥ 1 mg/L 5%/4%; cefotaxime MIC ≥ 2 mg/L 0.4%/0%; erythromycin 29%/22%, tetracycline 18%/23%; trimethoprim-sulfamethoxazole (SXT) 37%/45%. However we observed a decrease in the number of cases of IPD associated with resistance (n pre-PCV13/n post-PCV13): penicillin (131/67), cefotaxime (18/8), erythromycin (110/49), tetracycline (67/52), SXT (139/102). The increase in SXT resistance was significant. All isolates were susceptible to chloramphenicol, levofloxacin, rifampicin and vancomycin.

Conclusions: Although PCV13 was recently introduced into the immunization schedule, we observed decrease in PCV13 serotypes in <2 years old group and associated resistance. Surveillance is needed to continue monitoring the impact of PCV13-vaccination program.