ANTIMICROBIAL RESISTANCE DETERMINANTS AND SUSCEPTIBILITY PROFILES OF PNEUMOCOCCAL CARRIAGE ISOLATES RECOVERED FROM HEALTHY CHILDREN IN PERU PRE-PCV INTRODUCTION

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Background

- Nasopharyngeal colonization by *S. pneumoniae* is common. In circumstances of crowding (e.g. daycare centers, hospitals), the risk of colonization with pneumococci is high (1).
- Pneumococcal resistance to antimicrobial agents has evolved into a worldwide health problem. PCV7 had a limited effect on resistance, while introduction of PCV13 resulted in a significant decline in carriage of antibiotic non-susceptible pneumococci (1-3).
- The aim of this study was to examine the susceptibility profiles of pneumococcal isolates carried by children in Peru pre-PCV7 introduction

Methods

DNA was extracted from 522 carriage isolates obtained from children under 2 years old in 3 different regions of Peru between 2007 and 2009: the coast (Lima, Piura, n=305), the sierra (Cusco, Abancay, Arequipa, Huancayo, n=152), and the amazon basin (Iquitos, n=65). Whole genome sequencing was performed as part of the Global Pneumococcal Sequencing project (www.pneumogen.net). Sequences were analyzed using the CDC's *Streptococcus* lab pneumococcal typing pipeline. Non-susceptibility to 6 different β-lactams was predicted by assigning a PBP type as previously described (4). Contingency tables and a chi-squared test (or a Fisher's exact test) were used to determine significance of associations.

Results and discussion

Four hundred and thirteen (80%) isolates were predicted to be non-susceptible to at least one antimicrobial class, including 160 (31%) isolates resistant to at least three classes (multidrug resistance, MDR). The highest rates of non-susceptibility (NS) were observed against co-trimoxazole and penicillin (Table 1). The coastal region had the highest proportion of multidrug resistant isolates, significantly higher (p=0.04) than in the amazon basin and the sierra (Figure 1). Daycare attendance, having 2 or more siblings, and antibiotic use at the time of collection, were all associated with multidrug resistance (Table 2). As expected, there was a strong association between PCV7-serotype and penicillin non-susceptibility (OR=7.7, p<0.001), as well as MDR. The lineages most commonly associated with PNS and MDR were: 19F/CC236(PMEN14) in the coast, 6B/CC90(PMEN2) in amazon basin, and 23F/CC81(PMEN1) in the sierra.

Conclusions

Since PCV7 contains 19F, 6B and 23F, their prevalence and associated MDR are likely to have decreased since the introduction of the vaccine.

Figure 1. Proportion of multidrug resistant isolates by region

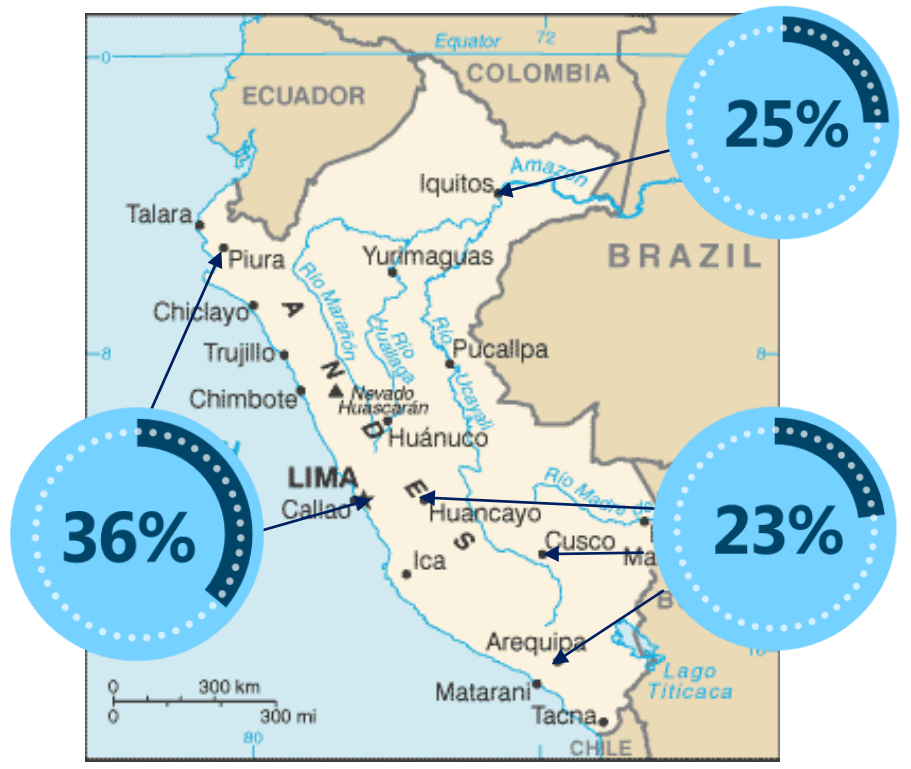

Table 2. Factors associated with multidrug resistance

	OR	p-value
Daycare attendance	4.17	0.002
2 or more siblings	2.00	0.006
Antibiotic use at collection	2.81	<0.001
Vaccine (PCV7) serotype	2.77	<0.001

References

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Table 1. Antibiotic non-susceptibility (NS) predicted by whole genome sequencing.

Antibiotic	Number of NS isolates (%)	Resistance determinants (n)	Predicted MIC Range
Penicillin	245 (47.1)	PBP genes	0.12-8.0
Amoxicillin	187 (35.9)	PBP genes	0.25-8.0
Meropenem	138 (26.5)	PBP genes	0.5-1.0
Cefotaxime	142 (27.3)	PBP genes	1.0
Ceftriaxone	146 (28.1)	PBP genes	1.0-4.0
Cefuroxime	154 (29.6)	PBP genes	1.0-2.0
Erythromycin	126 (24.1)	ermB (34), mef (59), ermB + mef (33)	
Clindamycin	67 (12.8)	ermB (34), ermB + mef (33)	
Cotrimoxazole	385 (73.8)	I100L substitution in folA (9), insertions in folP (110), or both (266)	
Tetracycline	164 (31.4)	tetM (164)	
Chloramphenicol	44 (84.3)	cat (44)	
Rifampin	4 (0.8)	H499N substitution (3) or H499Y substitution (1) in rpoB	

GPS Global Pneumococcal Sequencing Project

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