STREPTOCOCCUS PNEUMONIAE VACCINE SEROTYPES ACQUIRE PENICILLIN BINDING PROTEIN GENE MOSAICS FROM STREPTOCOCCUS MITIS (ID 428)

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Abstract

Background

Beta-lactam resistance in the pneumococcus remains a global concern, with countries reporting up to 80% penicillin resistance. Horizontal gene transfer (HGT) with closely related Streptococci generates mosaicism in penicillin-binding-protein (pbp) genes, alters beta-lactam binding, and reduces susceptibility. We hypothesised that HGT between S. mitis and S. pneumoniae results in reduced penicillin-susceptibility amongst vaccine-types.

Methods

We analysed 501 publicly available whole-genome sequences (168 S. mitis, 164 S. oralis, 169 S. pneumoniae). We extracted pbp1a, pbp2b, and pbp2x sequences, determined sequence diversity, and identified HGT using FastGEAR. We determined pneumococcal beta-lactam susceptibility using the CDC pipeline.

Results

Mosaic fragments in pbp1a, pbp2b, and pbp2x were identified in 34.3%, 35.5%, and 42.6% of pneumococci respectively. Most fragments (69.9-92.5%) were identified among transpeptidase binding regions, of which S. mitis contributed the most (56.9-60.5%) and had the greatest nucleotide diversity. Pneumococci with acquired transpeptidase fragments had reduced penicillin (MIC-2mg/L), amoxicillin (MIC-1.5mg/L), and cefotaxime (MIC-1mg/L) susceptibility. Pneumococci with S. mitis fragments had reduced beta-lactam susceptibility and included serotypes 6B (10/19), 19F (16/17), and 23F (9/13).

Conclusions

S. mitis is an important source of pbp diversity in S. pneumoniae and contributes to reduced beta-lactam susceptibility among vaccine-types. This may contribute to AMR emergence amongst pneumococcal lineages that escape vaccine control.