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Poster Session IV
Molecular epidemiology of Haemophilus, Moraxella, and Neisseria

GLOBAL PREVALENCE, GENETICS AND CLONAL RELATEDNESS OF MACROLIDE RESISTANCE IN MORAXELLA CATARRHALIS (2010-2012)

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Objective: To evaluate the global prevalence of macrolide resistance (MAC-R) in *Moraxella catarrhalis* during 2010 to 2012 and to determine the genetic basis of resistance and clonal relatedness of strains. MAC-R is generally <1% in most regions of the world but is known to be higher in the Asia Pacific region, especially in China.

Methods: Susceptibility testing was performed using Clinical and Laboratory Standards Institute (CLSI) broth microdilution methodology on 2,366 isolates isolated in 2010 (853 isolates), 2011 (771 isolates) and 2012 (742 isolates). Isolates were from 169 medical centers in 35 countries in the European Union (671 isolates), United States (USA; 1214 isolates), Latin America (117 isolates), and Asia-Pacific region (APAC; 364 isolates). A total of 21 isolates were non-susceptible to clarithromycin (>=2 mg/L, CLSI M45-A2 criteria) and 20 of these strains were available for further testing (one isolate from UK could not be recovered from storage). Known methylase- and efflux-encoding genes were investigated using PCR. Ribosomal protein L4 and L22 genes and 23S rRNA (each of 4 alleles) were sequenced. Clonality was assessed by PFGE using SpeI.

Results: Overall, 21/2366 (0.9%) of isolates were macrolide resistant. In China, 17/105 (16.2%) of isolates were macrolide resistant with the four remaining isolates found in Korea, New Zealand (NZ), UK and USA. No isolates were positive for the methylase or efflux genes tested. The most prevalent resistance mechanism (15 isolates) was A2058T mutation in all 4 23S rRNA gene alleles in 6 cities in China (13 isolates) and one isolate in Korea. PFGE patterns showed diverse clonality but with some isolates being identical within and between cities. A2058T (4 alleles) was associated with high level clarithromycin (512-2048 mg/L) and azithromycin (128-512 mg/L) resistance. Three isolates (all same city in China with identical PFGE patterns) possessed A2059T 23S rRNA gene mutations (4 alleles) combined with an L22 K68T amino acid substitution and demonstrated low-level MAC-R (clarithromycin and azithromycin <=4 mg/L). One strain from USA had a P87_R88 RAMP insertion in L22 with low-level MAC-R and one strain from NZ had A2058T (4 alleles) combined with L22 K68T and showed high-level MAC-R.

Conclusions: Overall MAC-R in *M. catarrhalis* was low (0.9%) but much higher in the APAC region, primarily due to high MAC-R (16.2%) from multiple sites in China. The majority of the Chinese isolates and the Korean isolate demonstrated high level MAC-R and had a common mechanism of resistance (A2058T in all 4 alleles) and some evidence of clonality between and within cities. Other mutations were associated with low-level MAC-R and were either clonal (the 3 Chinese isolates) or not related to each other or any of the other strains (the NZ and USA single isolates).