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Poster Session III

Tuberculosis: clinical observations

EPIDEMIOLOGY OF TUBERCULOSIS: INVESTIGATION FROM THREE GEOGRAPHICAL AREAS IN GREECE

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Objectives. To investigate the epidemiology of tuberculosis from three distinct regions in Greece including molecular typing of isolates.

Methods. Demographic, clinical and laboratory data of 211 consecutive tuberculosis patients (111: Athens metropolitan area, 50: Thessaly [Central Greece], 50: Crete [Southern Greece]) were recorded. Patients were diagnosed during 2006-2011. Strains were genotyped using the Mycobacterial Interspersed Repetitive Units-Variable Number of Tandem Repeats (?IRU-VNTR) method by analyzing 24 polymorphic loci. The corresponding lineage of *M. tuberculosis* (MTB) was determined using the MIRU-VNTRplus database (<http://miru-vntrplus.org>).

Results. Among 211 patients, 124 were males (58.8%). The majority (146/211 patients; 69.2%) were Greeks (Athens: 69%, Thessaly: 82%, Crete: 56%, $p=0.019$) with higher mean age compared to foreigners (62.8 versus 31 years, $p<0.001$). Among Greeks, 36% were aged <60 years indicating continuing transmission in the community. Foreign patients originated mostly from Eastern Europe and Asia (84.6%). Pulmonary disease was diagnosed among 100/146 Greek (68.5%) and 50/65 foreign patients (76.9%). Isolates were identified as *Mycobacterium tuberculosis* ($n=206$), *M. bovis* BCG ($n=3$), *M. bovis* ($n=1$), and *M. africanum* ($n=1$). Resistance rates were: isoniazid 8.5% (range among regions: 8-10%), rifampin 1.4% (0-2%), ethambutol 0.05% (0-3%), streptomycin 7.6% (2-12%) and pyrazinamide 4.7% (2-8%). Only three strains (1.5%) were multidrug-resistant (MDR). By MIRU-VNTR analysis 187 distinct genotypes were identified and a total of 24 isolates (11.4%) were grouped into 10 clusters (cluster size: 2-4). Laboratory contamination was assumed in 4 cases (1.8%). Two suspected incidences of intrafamilial transmission were confirmed (6 patients in total, of which 4 were children). Among the rest of clustered cases (14 cases) no geographical link could be demonstrated. MIRU-VNTR classified 50% of isolates (Athens: 52%, Thessaly: 56%, Crete: 40%) in 12 *M. tuberculosis* families. Most frequent were Harlem (12%), S (12%), Delhi/CAS (7%) and LAM (5%). Harlem and S families were detected among both Greeks and foreigners (10.3% versus 15.4%, and 12.3% versus 10.8%, respectively), while Delhi/CAS was isolated exclusively among foreigners (21.5%). Eleven strains (5%) belonged to the Beijing family. They were recovered from all three regions (Athens: 8/111, Thessaly: 2/50, Crete: 1/50) demonstrating frequencies of 3.6% in Greeks and 12% in foreigners ($p=0.08$). Among the three MDR isolates, two were Beijing strains.

Conclusion. Apart from Crete, tuberculosis is still more frequently diagnosed among Greeks but not exclusively linked to increased age. MDR strains remain uncommon and are associated with the virulent Beijing type. A considerable isoniazid resistance rate appears constant between regions. This finding in connection to low MDR rates justifies the application of rapid molecular testing targeting isoniazid rather than rifampin resistance genes. The application of genotyping for the first time forms a basis for the delineation of molecular epidemiology of MTB in Greece.