EPIDEMIOLOGY AND DRUG RESISTANCE PATTERN OF MDR TB IN ITALY

D.M. Cirillo [1], E. Borroni [1]
[1]*Ospedale San Raffaele*

Multidrug-resistant (MDR) and extensively drug-resistant (XDR-TB) TB represent a major threat for global TB control. In 2015 and 2016 respectively, 70/2609 and 70/2666, culture confirmed Multi Drug Resistant (MDR) cases were notified. Sixteen Extensively Drug Resistant (XDR) cases were also detected among the 119 (out of the 140 MDR) tested for resistance to second line drugs. The majority of cases were diagnosed in foreign born population. Molecular epidemiological studies show that local and global MDR/XDR-TB epidemics are driven by transmission rather than stepwise acquisition of resistance due to incorrect therapy. Tracing the transmission by discriminatory molecular tools allows to design the best strategies to control the epidemic at the local level and to identify cross border clusters. Over the past 15 year the European Centre for Disease Prevention and Control (ECDC) has supported initiates to trace the MDR/XDR TB epidemic at the EU level by the best available molecular tools. The recent evidences show that Whole Genome Sequencing based on NGS technology has the capacity to provide highly reliable information on drug resistance prediction and on transmission. Standardization of the analysis allows comparing data worldwide providing support for cross-border cluster identification. In 2016-17 a large cluster among Somali migrants has been identified in several EU countries. Two cases belonging to this cluster have been identified in Italy in response to ECDC request for investigation. In September 2017 ECDC has launched a 30 program, on the use of WGS for molecular typing and characterization of M. tuberculosis in the EU/EEA. The study is coordinated by the EUSeqMyTB consortium lead by Italy and represents a major step forward towards the effective implementation of genomic-based typing as the reference method for MDR/XDR-TB surveillance within the EU/EEA context. In 2016, as many other EU Countries we have started using NGS based technology to study cluster transmission and to provide guidance for clinical management of DR cases. We have performed a total of 295 WGS of MDR/XDR strains collected in Italy since 2012. For 175 of them we have performed mic to 12 drugs including new drugs (bedaquiline and delamanid). Of those 47% were MDR, 15% XDR and very few rifampicin resistant only. 17% were preXDR based on resistance to second line injectable and 14% based on fluoroquinolone resistance. Pattern of mutations was compared to mic distribution for each drugs and confirmed that the critical concentration recommended for some drugs are not appropriate and need to be revised. In addition we confirmed that there is not pre-exposure high level resistance to Bedaquiline while for Delamanid this has been documented. The most prevalent lineages are Beijing, Euro-American and LAM. Our data show that MDR transmission is occurring in the country and is not limited to any particular lineage. Although the majority of MDR clusters includes foreign born or italian born cases only ,evidences of mixed cluster have identified.