

# Clinical, epidemiological, and genetic features of human *Mycobacterium avium*, *Mycobacterium intracellulare* and *Mycobacterium chimaera* strains isolated in Tuscany, Italy, from 2004 to 2019

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**Introduction:** *Mycobacterium avium* complex (MAC) is a group of nontuberculous mycobacteria responsible for most of the human-associated infections. Recently, the high emergence of MAC human diseases has attracted increased attention worldwide. MAC predominantly consists of *Mycobacterium avium* and *Mycobacterium intracellulare* that are implicated in a wide spectrum of clinical manifestations, including respiratory tract infections, lymphadenitis in children and disseminated infections in severely immunocompromised patients. *Mycobacterium chimaera* has been recently involved in a global outbreak of infection related to heat-cooler unit contamination. The aim of the present study is to provide the clinical, epidemiological and genetic characterization of MAC clinical strains isolated in Tuscany, Italy, over the last 16 years.

**Materials and Methods:** A total of 171 MAC strains, identified by InnoLipa probes, were collected from 2004 to 2019 in the Laboratory of Clinical Mycobacteriology of the University Hospital of Pisa, Italy. The minimum inhibitory concentration (MIC), determined by broth microdilution assay, was used to evaluate the drug susceptibility against several drugs, including clarithromycin. Variable numbers of tandem repeats (VNTR) typing was performed to genotype *M. avium* and *M. intracellulare*.

**Results:** Of the 171 MAC isolates, 113 were *M. avium*, 50 were *M. intracellulare* and 8 were *M. chimaera*. MAC strains were prevalently isolated from subjects older than 65 years (51%), in whom the infection occurred primarily at the lung level. *M. intracellulare* and *M. chimaera* were isolated almost exclusively from respiratory samples (90%); of the *M. avium* isolates, 79% were from respiratory specimens, 10% from lymph nodes, 4,5% from blood and the remaining 6,5% from other clinical specimens. We found that most MAC isolates, including all the *M. chimaera* strains, were susceptible to clarithromycin; only 5 isolates of *M. avium* and 1 isolate of *M. intracellulare* were resistant to clarithromycin. The results obtained by the VNTR analysis showed that *M. avium* isolates displayed a high degree of genetic relatedness, whereas *M. intracellulare* isolates did not show a close genetic relationship.

**Discussion and conclusions:** The characterization of the MAC clinical isolates of the last sixteen years showed that *M. avium* was the most abundant organism, followed by *M. intracellulare*. *M. chimaera* strains were exclusively associated with pulmonary infections and not with endocarditis or disseminated infections after cardiac surgery. The findings from the molecular analysis indicated that strains of *M. avium*, but not *M. intracellulare*, exhibit a high phylogenetic proximity, suggesting that MAC strains may have different sources and route of transmission.