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Molecular epidemiology study of *Mycobacterium tuberculosis* and its susceptibility to anti-tuberculosis drugs in Indonesia

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Abstract

Background: Genotyping of *Mycobacterium tuberculosis* helps to understand the molecular epidemiology of tuberculosis and to address evolutionary questions about the disease spread. Certain genotypes also have implications for the spread of infection and treatment. Indonesia is a very diverse country with a population with multiple ethnicities and cultures and a history of many trade and tourism routes. This study describes the first attempt to map the molecular epidemiology of TB in the Indonesian archipelago.

Method: From 2008 to 2011, 404 clinical specimens from sputum-smear (SS+) TB patients, age \geq 15 years, were collected from 16 TB referral primary health centers (PHC) in 16 provincial capitals in Indonesia. Susceptibility testing to first line drugs was conducted for 262 samples using the agar proportion method as per WHO guidelines. Spoligotyping was done on all samples.

Results: Ninety-three of the 404 samples (23 %) were from the Beijing family, making it the predominant family in the country. However, the geographic distribution of the family varied by region with 86/294 (29.3 %) in the western region, 6/72 (8.3 %) in the central region, and 2/72 (2.8 %) in the eastern region (p < 0.001). The predominant genotype in the central and eastern regions was from the East-African-Indian (EAI) family, comprising 15.3 % (11/72), and 26.3 % (10/38) of the isolates, respectively. Drug susceptibility to first-line anti-TB drugs was tested in 262 isolates. 162 (61.8 %) isolates were susceptible to all TB drugs, 70 (26.7 %) were mono-resistant 16 (6.1 %) were poly-resistant, and 14 (5.4 %) were multi-drug resistant (MDR). The proportion of Beijing family isolates in the susceptible, mono-resistant, poly-resistant, and MDR groups was 33/162 (20.4 %), 28/70 (40.0 %), 6/16 (37.5 %), and 3/14 (21.4 %), respectively. Overall, resistance of the Beijing family isolates to any of the first line TB drugs was significantly higher than non-Beijing families [37/71 (52.1 %) vs. 63/191 (33.0 %) (p-value = 0.003)].

Conclusion: The distribution of *Mycobacterium tuberculosis* genotypes in Indonesia showed high genetic diversity and tended to vary by geographic regions. Drug susceptibility testing confirmed that the Beijing family of *M.tb* in Indonesia exhibited greater resistance to first line anti-TB drugs than did other families.

Background

Tuberculosis (TB) remains a major global health problem and ranks as the second leading cause of death from an infectious disease worldwide. There were 9 million new TB cases and 1.5 million TB related deaths in 2013. Among these deaths, it was estimated that more than 200,000 were due to MDR-TB, a high proportion of the

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Indonesia is considered a high-burden country for TB, ranked fifth in TB incidence (460,000 new TB patients each year) worldwide [1]. An Indonesian National Basic Health Survey in 2010 reported 289 cases/100,000

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