

Venue: GIZA
23rd August 2007
1100-1215 hr

Symposium 5C: Symposium on Tuberculosis

S5C-1. MDR tuberculosis in Indonesia: Importance for standardization before XDR widespread

Lia Gardenia Partakusuma

Indonesian Association of Clinical Pathologists, Persahabatan Hospital and National TB Lab Working Group, Indonesia

One of significant public problem in number of countries is the emergence of resistance to drugs used to treat tuberculosis (TB) or particularly multidrug resistant TB (MDR-TB). The incidence of drug resistance has increased since the first drug treatment for TB was introduced in 1943 and followed the widespread use of rifampicin since the 1970s. The first time standardized information on drug resistance from surveys or surveillance system conducted since 1994 in 35 countries. WHO and the International Against Tuberculosis and Lung Disease (IUATLD) reported those data in 1997. This information confirmed what many had feared: drug resistance was widespread and MDR-TB was at a critically high level in some parts of the world. Nowadays, Extremely Drug Resistant (XDR) cases found in several countries and cause more difficulties in decreasing morbidity and mortality in TB. From a microbiological perspective, resistance is caused by genetic mutation that makes a drug ineffective against the mutant bacilli. Ongoing transmission of established drug-resistant strains in a population is also a significant source of new drug-resistant cases. Standardized Drug Sensitivity Test (DST) of at least isoniazid and rifampicin is needed in any program to control drug-resistant TB. Once DST of first line drugs operates at a consistently high level of proficiency, laboratories serving populations and patients with significant previous exposure to second-line drugs may consider extending their services to DST of second-line drugs. Detection and treatment of all forms of TB, including drug-resistant forms, should be standardized and integrated within national TB control programs. Starting from mid 2006, Persahabatan Laboratory and several provincial laboratories supervised by IMVS Laboratory, Adelaide, Australia, supra national reference laboratory under National TB Program to improve quality assurance for culture and sensitivity test. Proficiency test for drug sensitivity test has done in 2006 - 2007. Also we participated Quality Control Program from Thailand TB reference laboratory for smear, culture and drug sensitivity test. Surveillance for drug resistance has ongoing in Indonesia. Keyword: MDR-XDR, Indonesia, Persahabatan Lab, Quality Assurance, DST.

S5C-2. Molecular epidemiology of *Mycobacterium tuberculosis* in Indonesia: A predominance of Beijing genotype strains and its clinical significance

Ida Parwati

Consultant Clinical Pathologist, Bandung, Indonesia

Molecular typing of *Mycobacterium tuberculosis* has shown as a powerful tool for molecular epidemiology as a complimentary to conventional epidemiology. This technique use to characterize the strains of *M. tuberculosis* circulating in given area, to investigate transmission, outbreak, laboratory cross contamination, and to discriminate reinfection versus reactivation of TB. In recent years there was a high prevalence and worldwide spreading of *M. tuberculosis* Beijing genotype. Studies in animal model have shown that Beijing strains are more virulent, however little is known about clinical evidence of increased virulence. We examined the prevalence of Beijing genotype by spoligotyping

and its association with clinical presentation in pulmonary tuberculosis (PTB) patients. A total of 633 consecutive PTB patients with positive culture of *M. tuberculosis* were spoligotyped. DNA extracted from *M. tuberculosis* colonies were amplified using primers: DRa: 5'-GGT TTT GGG TCT GAC GAC-3', biotinylated at 5' end and DRb : 5'-CCG AGA GGG GAC GGA AAC-3'. PCR products were hybridized by reverse line blotting technique to Biodyne C membrane which contains immobilized 43 spacers oligoprobes. Beijing genotype was defined as spoligopattern showing hybridization to spacer 35-43, other patterns were grouped into non-Beijing genotype. Clinical characteristics, bacteriological results and treatment outcome were compared between patients infected by *M. tuberculosis* Beijing and non-Beijing genotype. *M. tuberculosis* Beijing genotypes were detected in 33.5% of PTB patients. Patients infected by *M. tuberculosis* Beijing genotype showed more night-sweats (OR 1.74, 95% CI 1.2-2.6), advanced chest X-rays presentation with more cavitation (OR 3.24 95% CI 2.1-5.1), more sputum mycobacterial load (OR 1.53, 95% CI, 1.1-2.2) and bacterial persistent to TB treatment (OR 2.54, 95% CI, 1.3-5.1). *M. tuberculosis* Beijing genotypes were the most prevalent strain in Indonesia, and more virulent compared to non-Beijing genotype.

S5C-3. Rapid tuberculosis diagnostic test developed in the Department of Clinical Pathology, Dr Soetomo Hospital, Surabaya

Jusak Nugraha, Yolanda Probohoesodo, Indro Handojo

Department of Clinical Pathology, Dr Soetomo Hospital/Medical Faculty Airlangga University, Surabaya, Indonesia

Development of rapid methods for mycobacterial species identification and drug susceptibility testing has become especially important because of the extremely rapid progression of tuberculosis in human immunodeficiency virus (HIV)-positive individuals and also due to the growing rates of drug resistance. Our rapid detection of TB has begun in 1988 when a serological test called PAP-TB was developed by Handojo. An action of perfecting this test was performed in 1995 by changing the PAP-TB into TB-DOT, which is simpler and faster. This test has a sensitivity of 88.9% and specificity of 87.5%. In order to increase the specificity and sensitivity of the serological test, an epitope mapping of ESAT-6 antigen was performed by Nuha in order to find the specific epitopes for Indonesian people (2005). Our attempt now is focused on rapid identification of Mycobacteria from patient specimen using PCR method and detection of drug resistance using PCR-SSCP. Preliminary results show a sensitivity and specificity of 100% and 100% respectively to detect Mycobacterium complex. The research is still going on with larger samples. To detect latent-TB, a commercial test for measuring IFN- γ production in whole blood (Quantiferon-TB) was chosen. As a test for measuring degree activity of pulmonary tuberculosis, level of IL-18 sera were measured using ELISA method, especially for patients with a negative smear and paucibacillary diseases. These results are still being further investigated.