


Advances in Biomolecular Medicine

Editors

Robert Hofstra
Noriyuki Koibuchi
Suthat Fucharoen



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Mycobacterium tuberculosis load and rifampicin concentration as risk factors of sputum conversion failure

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ABSTRACT: Pulmonary TB is a chronic infectious disease that has become a global health burden. The aim of this study is to understand the role of bacterial load and plasma rifampicin concentration as risk factors of sputum conversion failure in pulmonary TB. This is a quantitative study with a cross-sectional design conducted on 102 subjects. The study was conducted at the RSP Faculty of Medicine, Universitas Padjadjaran. Plasma rifampicin concentration was measured using UPLC, sputum conversion was examined by Ziehl–Neelsen staining, and statistical analysis was performed using SPSS version 20. The results indicate that the baseline *Mycobacterium tuberculosis* (M.tb) load was significantly different between the groups ($p = 0.04$), and high M.tb load was the risk factor of sputum conversion failure (POR = 2.97 CI 95% = 1.23–7.15, $p = 0.015$). In conclusion, M.tb load was found to be the risk factor of sputum conversion failure, not the plasma rifampicin concentration.

1 INTRODUCTION

Pulmonary TB is a chronic infectious disease caused by *Mycobacterium tuberculosis* (M.tb), which has become a global health burden. M.tb typically affects the lungs (pulmonary TB) as well as any other organ of the body (extra-pulmonary TB). The disease spreads when individuals with pulmonary TB expel bacteria into the air, for example, by coughing. Overall, a relatively small proportion (5–15%) of the estimated 2–3 billion people infected with M.tb will develop the TB disease during their lifetime. In 2015, an estimated number of 10.4 million new (incident) TB cases were reported worldwide, of which 5.9 million (56%) were among men, 3.5 million (34%) among women, and 1.0 million (10%) among children. Six countries accounted for 60% of new cases: India, Indonesia, China, Nigeria, Pakistan, and South Africa. There were an estimated 1.4 million TB deaths in 2015. TB remained one of the top 10 causes of death worldwide in 2015. In the same year, 6.1 million new TB cases were reported to national authorities and the WHO. One of the diagnostic tests for TB is sputum smear microscopy. This diagnostic technique for tuberculosis was developed more than 100 years ago. Sputum samples are examined under a microscope to determine whether bacteria are present. In the current case definitions recommended by the WHO, one positive result is required for a diagnosis of smear-positive pulmonary TB (WHO 2016).

Sputum smear microscopy has been the primary method for the diagnosis of pulmonary tuberculosis in low- and middle-income countries, where about 95 per cent of TB cases and 98 per cent of TB deaths occur. It is a simple, rapid, and inexpensive technique that is highly specific in areas with a very high prevalence of tuberculosis. It also identifies the most infectious patients and is widely applicable in various populations with different socio-economic levels. Hence, it has been an integral part of the global strategy for TB control. However, sputum smear microscopy has significant limitations in its performance. The sensitivity is grossly compromised when the bacterial load is less than 10,000 organisms/ml sputum sample (Desikan 2013). A previous study has revealed that bacterial load is association with sputum conversion failure at 2 months after initiation of treatment. Some studies have reported that one of the risks of a persistent positive smear at 2 months was greater in patients with a bacterial load >3+ (Mota et al. 2012). Without appropriate treatment, the death rate from TB is high. Studies of the natural history of the TB disease in the absence of treatment with anti-TB drugs (which were conducted before drug treatments became available) have found that about 70% of people with sputum smear-positive pulmonary TB died within 10 years, as did about 20% of people with culture-positive (but smear-negative) pulmonary TB. Effective drug treatments were first developed in the 1940s.