ISONIAZID AND RIFAMPICIN RESISTANCE AND PATIENT TREATMENT RESPONSE IN A TUBERCULOSIS AND HIV-1 CO-ENDEMIC POPULATION IN WESTERN KENYA IN 2012-2014

ABSTRACT

In 2015, 10.4 million people worldwide had tuberculosis (TB) and 1.4 million deaths occurred, 400 000 of whom were HIV-positive, Sub-Saharan Africa (SSA) accounted for 81% of these cases. In 2015, 480 000 new cases of multi-drug resistant TB (MDR-TB) were detected globally. In Kenya, in 2015, 107 000 people had TB and 36 000 were HIV co-infected. In western Kenya, the prevalence of TB and HIV in 2015 was 39.2% and 15.1%, respectively and in 2008, 10 cases of MDR-TB occurred. Patients with HIV have a deficient immune system and are likely to be TB co-infected. As a result of the pill burden of anti-retroviral and TB therapy, poor adherence may occur. Rifampicin (RIF) and isoniazid (INH) are first-line anti-TB drugs. Resistance to INH is associated with mutations on the *kat* G and *inh* A genes while *rpo* B gene mutations lead to RIF résistance. Multi-drug resistant TB arises after acquisition of either INH or RIF resistance followed by resistance to the companion drug. Patients with resistant TB require admission which increases transmission. Methods for determining drug resistant TB includes drug susceptibility tests (DST), GeneXpert, Line probe assay (LPA) and sequencing. In western Kenya, current data on the distribution of RIF and INH mutations is not available. In addition, the association of drug resistant mutations with HIV and the treatment response of HIV infected and uninfected patients with TB are not known. As such, the objectives of the current study were to determine the proportion of drug resistant *Mycobacterium tuberculosis* in sputum isolates and investigate the association of RIF and INH gene mutations with HIV status and monitor treatment response in a TB/HIV co-endemic population in western Kenya. The present study was longitudinal in which enrollment was done between 2012 and 2014 after the revision of the TB treatment regimen and patients with confirmed drug resistant TB were followed up for one year to establish the TB treatment response as confirmed by sputum smear microscopy. Random sampling of 415 facilities that support routine TB diagnosis in 13 counties in western Kenya was done. Patients with suspected TB symptoms and Ziehl-Neelsen (ZN) positive patients were targeted for enrollment. A total of 1381 new and 18 previously treated TB patients were enrolled. HIV infected patients accounted for 61% of the enrolled participants. Sputum samples were cultured on *Mycobacteria* growth indicator tubes (MGIT), DST and LPA performed to identify drug resistance and specific mutations on the *rpo* B, *kat* G and *inh* A genes. Discordant samples were sequenced. Conversion rate was calculated by finding the percentage of smear negative and positive patients at follow-up and initial visit, respectively. Proportion of mutations as estimated by LPA and DST was as follows: MDR-TB, 0.95%, 1.53%; RIF mono-resistant TB, 0.88%, 0.66%; INH mono-resistant TB, 1.83%, 1.97%, respectively. Regression analysis showed that RIF resistance was associated with HIV status (P = 0.025). Mann-Whitney tests revealed that the conversion time of HIV infected and uninfected patients with TB drug mutations was comparable (P = 0.180). The results of the study showed that INH mono-resistance was common. Detection of INH mono-resistance in TB endemic areas should be scaled-up as well as TB contact investigation studies to increase early detection of resistant strains.