
Abstract:
Reducing mortality from HIV-associated tuberculosis (TB) requires diagnostic tools that are rapid and have high sensitivity among patients with poor prognosis. We determined the relationship between disease severity and the sensitivity of new sputum-based and urine-based diagnostic assays. Consecutive ambulatory patients enrolling for antiretroviral treatment in South Africa were screened for TB regardless of symptoms using diagnostic assays prospectively applied to sputum (fluorescence smear microscopy, Xpert MTB/RIF and liquid culture (reference standard)) and retrospectively applied to stored urine samples (Determine TB-LAM and Xpert MTB/RIF). Assay sensitivities were calculated stratified according to pre-defined indices of disease severity: CD4 count, symptom intensity, serum C-reactive protein (CRP), hemoglobin concentration and vital status at 90 days. Sputum culture-positive TB was diagnosed in 15% (89/602) of patients screened and data from 86 patients were analyzed (median CD4 count, 131 cells/µL) including 6 (7%) who died. The sensitivity of sputum microscopy was 26.7% overall and varied relatively little with disease severity. In marked contrast, the sensitivities of urine-based and sputum-based diagnosis using Determine TB-LAM and Xpert MTB/RIF assays were substantially greater in sub-groups.
with poorer prognosis. Rapid diagnosis from sputum and/or urine samples was possible in >80% of patients in sub-groups with poor prognosis as defined by either CD4 counts < 200 mg/L or hemoglobin < 8.0 g/dl. Retrospective testing of urine samples with Determine TB-LAM correctly identified all those with TB who died. The sensitivities of Xpert MTB/RIF and Determine TB-LAM for HIV-associated TB were highest among HIV-infected patients with the most advanced disease and poorest prognostic characteristics. These data provide strong justification for large-scale intervention studies that assess the impact on survival of screening using these new sputum-based and urine-based diagnostic approaches.