Abstract

Tuberculosis (TB) and HIV co-infections have a global prevalence with high morbidity and mortality and Africa is the worst hit. The HIV and AIDS has profound impact on the TB epidemic in Kenya, where up to 60% of TB patients are likely to be HIV co-infected and the mortality rate attributed to TB. Lack of diagnostic capacity has been a major barrier preventing an effective management of HIV-associated and drug resistant tuberculosis (TB). Microscopy is the gold standard for TB diagnosis and have various limitations. Molecular diagnostic methods are more specific and sensitive and have been applied in TB diagnosis. The *Mycobacterium tuberculosis*/Rifampin (Xpert MTB/RIF) assay is a rapid diagnostic tool that can simultaneously identify *M. tuberculosis* DNA and resistance to rifampin by nucleic acid amplification technique (NAAT). Urine lipoarabinomannan (LAM) antigen strip test is a rapid diagnostic tool that can detect LAM in antigenic form in the urine in patients with active TB. There is need to generate data to support recommendations for use of the assays for testing non-sputum clinical samples in African population especially in Western Kenya where currently there is a big problem in TB management. Urine as a biological sample for diagnostic testing is easy to collect, readily available and has a low infection risk to staff during collection. This study determined the optimal parameters (Zn, CD4+, Hb, Creatinine, proteinuria, hematuria), specificity and sensitivity for urine Xpert MTB/RIF assay and LAM strip test for diagnosis of tuberculosis using urine from HIV patients with active TB. This was a cross-sectional study in which 157 study participants were prospectively recruited. Normality tests were conducted using Shapiro and Wilks methods. The test for association between categorical variables was conducted using Pearson's Chi Square test. For skewed variables, a two sample Wilcoxon rank sum test was used. Cohen's kappa statistic (k) test was used to measure the level of agreement between the Xpert MTB/RIF and LAM determine strip test. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of Expert MTB/RIF and LAM strip test were evaluated against the sputum microscopy method as a gold standard. About 55% were TB positive by sputum microscopy, Gene Xpert had 17(11%) of the patients positive with 94% and 6% being MTB detected low and medium, respectively. LAM strip test showed that 28% of the patients were TB positive. Radiology had 45% of the patients with infiltrates. Protein or blood in urine was significantly associated with TB positivity based on LAM strip determine test (48% vs 24%; p=0.021). The weighted kappa coefficient was 0.48 (95% CI=0.32-0.63; p<0.0001). Sensitivity of urine Xpert MTB/RIF against Sputum microscopy was 17%, with a positive predictive value of 29%. While the specificity of urine Xpert MTB/RIF against Sputum Microscopy was 91%, with a negative predictive value of 83%. Stratified by CD4 categories, the test was more sensitive (30% vs. 11%) and specific (92% vs. 89%) to CD4≤100 cells/mm3 compared to CD4>100 cells/mm3, respectively. Sensitivity and specificity of urine Gene Xpert MTB/RIF test compared to LAM strip test increased to 39% and 100%, respectively. The sensitivity of LAM determine strip test against Sputum Microscopy was 38%, with a positive predictive value of 25% while the specificity of LAM determine strip test against Sputum Microscopy was 74%, with a negative predictive value of 84%. Sensitivity increased to 60% for those with CD4≤100 cells/mm3 whereas the specificity slightly increased to 76% for those with CD4>100 cells/mm3. The comparison of urine LAM determine strip test against urine Xpert MTB/RIF and urine culture were similar and it increased the sensitivity and specificity to 100% and 81%, respectively. The plotted receiver operating characteristic (ROC) curve yielded an area under the curve (AUC) of 0.56 (95% CI=0.46-0.66) indicating that urine MTB/RIF® is not accurate when used alone. This study recommends that urine Xpert MTB/RIF® is a sensitive and specific tool for diagnosis of TB taking Zn, CD4 count, Proteinuria, and Hematuria as optimal parameters. Both Xpert MTB/RIF® and LAM can be used as an adjunct test for diagnosis of active TB using urine samples in combination with other tests in the diagnosis platform.