Title: Evaluation of genotype MTBDRPLUS assay as a screening tool for multi-drug resistant tuberculosis surveillance among patients at high risk in Nairobi

Author: Mburu, Margaret Ciina

Abstract: Multi-drug resistant tuberculosis (MDR-TB) has emerged as an important global public health threat. The Kenya tuberculosis program has continued to report MDR-TB cases since the year 2005 to date from patents failing first line tuberculosis (TB) treatment. The current MDR-TB diagnostic methods for drug susceptibility testing (DST) are lengthy, take 3 months and are only available in research and reference laboratories in Kenya. This laboratory diagnostic delay has been observed to contribute to spread, increased morbidity and mortality due to MDR-TB. A rapid molecular test such as GenoType®MTBDRplus that would detect the MDR-TB early and in county laboratories needed to be validated in Kenya. This study describes a cross-sectional study that was conducted in Nairobi county from September 2009 to September 2010 where the specimens from TB patients with a history of treatment failure were collected, packed safely and sent for laboratory analysis at Central Tuberculosis Reference Laboratory (CTRL). GenoType®MTBDRplus assay was evaluated against Mycobacteria Growth Indicator Tube (MGIT) DST as the gold standard. Data on patient's demographics, Human Immunodeficiency Virus (HI V) status and laboratory tests were obtained from the laboratory request forms and worksheets. The data was cleaned and analyzed using Statistical Analysis System (SAS) version 9.1. Chi-square statistic was used to establish association between variables and test study hypothesis. Accuracy of GenoType®MTBDRplus was determined by Kappa statistic, sensitivity, specificity and predictive values. A total of 457 specimens were collected from Kenyatta National Hospital (32), Blue House (21), Eastern Deanery AIDS Relief Program (89), Rhodes chest clinic (57), Kibera South (28) and Kangemi Health Center (10). The rest of the specimens were received from other sites during the study period. Of the 455 specimens with age and gender records, 303 (66.6%) were males and 152 (33.4%) were females. The median age was 32 years, the youngest and the oldest being males of 3 and 67 years respectively. Of the 457 specimens with sputum smear results, 274 (60.0%) were smear positive while the remaining 183 (40.0%) were smear negative. The age group of patients was shown to influence the occurrence of smear positive (P=O.OOII). Patients with HIV positive status were 0.27 times likely to be smear positive compared to those with HIV negative status with a 95% confidence interval of 0.14 to 0.50 and a p-value of 0.0001. Of the 451 specimens with TB culture results, 61 % had culture confirmed tuberculosis, out of which 22.4% were MDR- TB. Being smear positive was not associated with MDR-TB (P=0.3031). TB and HIV co-infection among the culture confirmed tuberculosis patients was 42% (P<O.OOOI). There was excellent agreement between MGIT DST and GenoType®MTBDRplus with a kappa statistic of 0.8902 and a confidence interval of 0.7684 to 1.0000 for sputum specimens. A kappa statistic of 0.9312 with confidence interval of 0.8647 to 0.9977 was obtained for the isolates from Lowenstein media. Nairobi county has high rates of MDR-TB among patients with a history of first line anti-TB treatment failure. GenoType®MTBDRplus assay has been validated as a rapid and reliable method for surveillance ofMDR:TB in Nairobi, Kenya. The Kenya TB program should consider use of GenoType®MTBDRplus as a rapid test for diagnosing and surveIllance of MDR-TB in Nairobi county; accelerate MDR-TB case finding, care and treatment of

identified cases. Further research may be needed to explore the cost associated with scaling up this new test to other counties in Kenya.