Performance Assessment of the GenoType®MTBDRplus Assay for Rapid Detection of Multidrug-Resistant Tuberculosis among Clinical Isolates in Low Tuberculosis Burden Setting

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Abstract

Introduction: New molecular assays for rapid Multidrug-Resistant Tuberculosis (MDR-TB) detection continue to be developed. Rwanda has recently introduced the line probe assay for early TB and MDR-TB diagnosis. We aimed to assess the performance of GenoType®MTBDRplus test before its implementation in the routine testing.

Methods: Sputum samples from suspected MDR-TB patients received and processed at Rwanda National Reference Laboratory from 2010-2012 were included in this study. The performance of Genotype®MTBDRplus assay was evaluated versus the standard phenotypic conventional Drug Susceptibility Testing (DST) on Lowenstein Jensen. Sensitivity, specificity and predictive values (positive and negative) were calculated. Statistical analyses were performed using Epi Info version 3.5.3. P-values were derived from χ² tests applying Fisher Exact where appropriate.

Results: A total of 1548 participants were enrolled in this study, 463 (29.9%) were from new patients and 1085 (70.1%) patients were from retreated patients. The GenoType®MTBDRplus assay correctly identified 37 of 39 Isoniazid resistant strains; 33 of 36 Rifampicin resistant; and 30 of 32 MDR-TB strains for both tests. Compared to the reference standard, the sensitivity of the Genotype®MTBDRplus assay was 94.8% (95% CI: 79.2-99.2%) to detect Isoniazid resistance, 91.7% (95% CI: 77.5-98.2%) for Rifampicin and 93.8% (95% CI: 79.2-99.2%) for the combination of both, MDR-TB. The specificity was 99.3% for Isoniazid, 98.6% for Rifampicin and 99% for MDR-TB. Positive Predictive Value of Genotype®MTBDRplus assay was 96.8% for MDR-TB and its Negative Predictive value 98.8%. The GenoType®MTBDRplus performed well in identifying MDR-TB.

Conclusion: GenoType®MTBDRplus assay is a rapid and reliable test in detecting MDR-TB cases in Rwanda. Therefore, GenoType®MTBDRplus assay can be recommended for detecting MDR-TB in our setting to speed out MDR-TB detection in order to institute early treatment.

Keywords: GenoType®MTBDRplus assay; Multi-Drug Resistant Tuberculosis; Mycobacterium Tuberculosis complex; Drug Susceptibility Testing

Background

Tuberculosis (TB) especially Multi-Drug Resistant Tuberculosis (MDR-TB) is still considered as a major public health concern in developing countries. The World Health Organization (WHO) estimates that one third of world’s population is infected with TB whereby 9.2 million and 7.8 million of new TB patients occur annually in Asia and Sub-Saharan Africa. The spread of TB and MDR-TB was enhanced by the occurrence of HIV infection. The risk of developing TB is 5–15% per year in HIV-TB infected individuals (Global Tuberculosis Control [1,2]. About 14% of the global burden of new MDR-TB cases is found in Africa [3,4]. The internationally accepted gold standard for MDR-TB diagnosis is the detection of mycobacteria growth in cultures inoculated either on solid media Lowenstein Jensen (L-J medium) or liquid medium in Mycobacteria Growth Indicator Tube (MGIT; BACTEC MGIT960, Becton Dickinson, containing antibiotics even if it takes several weeks or months to obtain Drugs Susceptibility Tests (DST) results [3]. Due to delays in obtaining DST results to institute early treatment and case management, a rapid technique is needed to diagnose TB and MDR-TB. WHO recommends that countries should expand their capacity for culture-based DST and move to the new molecular based assays for diagnosing drug resistance [5,6].

In Rwanda, new molecular tools for rapid diagnosis of MDR-TB were recently introduced: as Genotype®MTBDRplus in 2010 and Xpert MTR/RIF in 2012. The GenoType®MTBDRplus assay has been used as a tool for early TB and MDR-TB diagnosis to support the Programmatic Management of Drug Resistant Tuberculosis in the country to institute early treatment. It has been shown that GenoType®MTBDRplus assay is the ideal technique to diagnose TB and MDR-TB and it accelerates the laboratory results for MDR-TB.
treatment and control [7,8]. Although the GenoType®MTBDRplus assay has been validated in different settings with high burden of tuberculosis like in Thailand, Asia and in Africa like in South Africa [7,9], there is a need to evaluate its performance to ensure the acceptable performance in other settings with low TB burden like Rwanda. We aimed to assess the performance of GenoType®MTBDRplus assay to detect Rifampicin and Isoniazid resistance. We compared its performance to the phenotypic drug susceptibility testing DST based method on L-J medium by assessing its sensitivity, specificity and predictive values (positive and negative) in diagnosing MDR-TB.

Material and Methods

Setting, population and design of the study

The present study was conducted at the National Reference Laboratory (NRL) located in Kigali city, Rwanda, in the Microbiology unit. The NRL is the main laboratory in the country which performs specialized tests for TB such as culture, DST, and molecular assay for early MDR-TB diagnosis. NRL acts also as a referral laboratory involved performing quality assurance in the TB network at quarterly basis for all district hospitals in the country. Between 2010 and 2012, GenoType®MTBDRplus assay was performed simultaneously on sputum specimens and clinical isolates obtained from 1548 patients from all district hospitals submitted to the NRL for routine culture and drug susceptibility testing to monitor MDR-TB. Sputum samples or Mycobacterium Tuberculosis Complex (MTBC) isolates obtained after inoculating L-J medium were used to detect drug susceptibility patterns. This study was conducted after getting ethical approval from School of Public Health.

A written permission was issued for allowing the researchers to conduct this research. Permission was obtained from the National Reference Laboratory and RBC/IHDFC/TB & Other Respiratory Diseases Divisions of Rwanda Biomedical Centre to carry out the laboratory analysis and get access to laboratory records. During the research work, the principle of respect for human dignity was taken into consideration. Testing was performed on residual portions of routine clinical specimens submitted for culture and conventional DST. Results were delinked from patient identifiers, and no patient names were collected. Therefore, informed consent was not being required for this study.

Samples preparation

Sputum samples from new patients or previously treated were digested and decontaminated using N-Acetyl-L-Cystein-Sodium Hydroxide (NALC-NaOH) method by adding an equal amount of NaOH-NALC solution to the sputum followed by washing using Prepared Phosphate Buffer Solution (PBS) [10]. Sputum sample concentration was done using a centrifuge for 15-20 minutes at 3000 x g in refrigerated aerosol free centrifuge cups. From the same decontaminated specimen two aliquots were made, one for inoculating L-J medium and the second one for DNA extraction to analyze the presence of mutations conferring resistance to Rifampicin (RIF) and Isoniazid (INH) by GenoType®MTBDRplus. The L-J medium was incubated at 37°C up to 8 weeks and inspected for growth every week as per NRL’s protocol. Positive culture underwent further laboratory testing to detect resistance pattern using both conventional DST by proportional method on L-J medium containing anti-TB drugs and GenoType®MTBDRplus Assay (Hain Lifescience GmbH, Nehren, Germany).

GenoType®MTBDRplus assay

The GenoType®MTBDRplus assay (Hain Lifescience GmbH, Nehren, Germany) was used according to the manufacturer’s instructions [11]. The performance of GenoType®MTBDRplus assay was evaluated by calculating its sensitivity, specificity and predictive values (positive and negative) versus the conventional phenotypic DST, proportion method on L-J medium.

Nucleic acid extraction

Deoxyribonucleic Acid (DNA) from decontaminated clinical specimens was extracted by thermal lysis and sonication following the manufacturer’s instructions test kits of GenoType®MTBDRplus assay. In brief, 500 μL of decontaminated sample was used for DNA extraction by physical method using thermal lysis and sonication and centrifugation at 13000 rpm at 4°C for 15 minutes; pellet were resuspended in 100 μL of sterile distilled water and mycobacteria were lysed by incubation at 95°C for 30 minutes and sonication for 15 minutes.

Master mix preparation

The main composition of Master Mix solution is hot star Taq polymerase enzyme in which PNM mix was added within a Polymerase Chain Reaction (PCR) buffer, Magnesium Chloride (MgCl₂) and hot grade water. The total reactions were given by the total number of specimens to be processed, plus one positive control (if culture), one negative control, two PCR controls (both negative and positive) and one extra correction volume.

Amplification

A 5-μL of lysate was used for amplification with the provided biotinylated primers. Two units (instead of 1 as reported in manufacturer’s instructions) of hot-start Taq DNA polymerase were used in the amplification step. The amplification was performed in a thermal cycler with a protocol consisting of 1 cycle at 95°C for 15 minutes (Taq activation cycle), 10 cycles of denaturation at 95°C for 30 seconds and 40 cycles of denaturation at 95°C for 25 seconds, primer annealing at 53°C for 40 seconds and extension at 70°C for 40 seconds, followed by a final extension at 70°C for 8 minutes.

Hybridization and detection

The GenoType®MTBDRplus assay is based on reverse hybridization between amplicons derived from a multiplex PCR and nitrocellulose-bound Wild-Type (WT) and Mutated (MUT) probes targeting the hotspot region of rpoB gene, the codon 315 of katG gene and the promoter region of inhA gene. The assay also includes amplification controls, and a control-probe for MTB complex DNA detection. Hybridization and washing was performed manually using the TWINCUBATOR® Hybridization Tray (Hain Lifesciences, Nehren, Germany) according to the manufacturer’s instructions [10,11].

Interpretation of results

To interpret the test results, the sheet provided with the purchased test kits where the test strip was aligned to the bands CC, AC and TUB
then observe for the presence or absence of wild type genes and the presence or absence of katG, inhA and rpoB genes mutation. Results were interpreted for susceptibility or resistance to RIF and INH according to manufacturer’s instructions. When using the evaluation sheet, the developed strips were pasted in the designated fields by aligning the bands CC, AC and TUB with the respective lines on the sheet. Determine the resistance status and write down in the respective column the appropriate results as shown in the example below (Figure 1).

**Conventional drug susceptibility testing method**

Conventional DST using proportional method known as Petroff method was used by inoculating L-J medium containing 20.0 μg and 40.0 μg of Rifampicin, 0.1 μg and 2.0 μg of Isoniazid. Both Rifampicin and Isoniazid were tested at high and low antibiotic concentration. A patient may be resistant at low antibiotic concentration or at high antibiotic concentration. To determine if an isolate is resistant, we first observe drug containing tube at each drug concentration and there should be no growth in the tube containing drug for an isolate to be susceptible. If there was growth, to determine whether an isolate is susceptible or resistant we compared with the control tube that contains the most diluted antibiotic of interest as described by Canetti et al., as follow: In case, the growth on the drug-containing tube is equal or more than the growth observed on the most diluted control tube $10^{-4}$, representing 1% of possible growth of a valid test, the isolate is considered as resistant. In case, growth on the drug-containing tube is less than the growth observed on the most diluted control tube $10^{-4}$, represents 1% of possible growth of a valid test, the isolate is considered to be susceptible for the specific drug as described elsewhere [12].

**Turnaround time of results**

Turnaround time was obtained by the difference between the time of the inoculation date of the test (conventional DST and/or GenoType® MTBDRplus test) and the date of the availability conventional DST results or the date of GenoType® MTBDRplus results from the computerized National Reference Laboratory database.

**Statistical methods**

Statistical analyses were performed using Epi Info version 3.5.3. P-values were derived from χ² tests applying Fisher Exact where appropriate.

**Results**

The GenoType® MTBDRplus assay was evaluated on 1548 specimens obtained from patients in which TB and MDR-TB was suspected. Out of 1548 samples tested by GenoType® MTBDRplus assay, 463 (29.9%) were from new patients and 1085 (70.1%) patients were from retreated patients. Moreover, out of 1548 samples included in this evaluation, 1106 (71.4%) were fresh sputum specimens and 442 (28.6%) were isolates from colonies harvested from L-J solid media (Table 1). Among sputum samples, the detection rate was 15.8% (175/1106) while 84.2% (931/1106) were negative for *Mycobacterium tuberculosis* Complex. In all isolates, culture positive from L-J medium, the detection rate of MTBC was found in 99.3% (439/442). In sputum samples, susceptibility patterns by GenoType® MTBDRplus assay show that INH was susceptible at the rate of 13.1% (145/1106) while MTB susceptible to RIF rate was 12.9% (143/1106). From isolates, patterns show that INH was susceptible at the rate of 79.8% (353/442) while Rifampicin sensitive in 78.7% (348/439) patients. Moreover, out of 1548 samples included in this evaluation, 1106 (71.4%) were fresh sputum specimens and 442 (28.6%) were isolates from colonies harvested from L-J solid media (Table 1). Among sputum samples, the detection rate was 15.8% (175/1106) while 84.2% (931/1106) were negative for *Mycobacterium tuberculosis* Complex. In all isolates, culture positive from L-J medium, the detection rate of MTBC was found in 99.3% (439/442). In sputum samples, susceptibility patterns by GenoType® MTBDRplus assay show that INH was susceptible at the rate of 13.1% (145/1106) while MTB susceptible to RIF rate was 12.9% (143/1106). From isolates, patterns show that INH was susceptible at the rate of 79.8% (353/442) while Rifampicin sensitive in 78.7% (348/439).

**Table 1: Resistance characteristics according to type of specimen analyzed by GenoType® MTBDRplus**

<table>
<thead>
<tr>
<th>Resistance characteristics</th>
<th>Type of specimens analyzed</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AFB+ Sputum n(%)</td>
<td>Isolates n(%)</td>
</tr>
<tr>
<td>All samples analyzed</td>
<td>1106 (71.4)</td>
<td>442 (28.6)</td>
</tr>
</tbody>
</table>

**Treatment history**

<table>
<thead>
<tr>
<th>Year</th>
<th>n</th>
<th>%</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>New</td>
<td>406(36.7)</td>
<td>57(13.0)</td>
<td>463(29.9)</td>
</tr>
<tr>
<td>Previously treated</td>
<td>700(63.3)</td>
<td>385(87.0)</td>
<td>1085(70.1)</td>
</tr>
<tr>
<td>Detection of MTBC</td>
<td>175 (15.8)</td>
<td>439 (99.3)</td>
<td>614 (39.7)</td>
</tr>
<tr>
<td>No detection, negative reaction</td>
<td>931 (84.2)</td>
<td>3 (0.7)</td>
<td>934 (60.3)</td>
</tr>
</tbody>
</table>

**Susceptible**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH</td>
<td>145 (13.1)</td>
<td>353 (79.8)</td>
</tr>
<tr>
<td>RIF</td>
<td>143 (12.9)</td>
<td>348 (78.7)</td>
</tr>
</tbody>
</table>

**Monoresistance**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH</td>
<td>30 (2.7)</td>
<td>86 (19.5)</td>
</tr>
<tr>
<td>RIF</td>
<td>32 (2.9)</td>
<td>91 (20.5)</td>
</tr>
</tbody>
</table>

**Multi Drug Resistance (MDR)**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH &amp; RIF</td>
<td>29 (2.6)</td>
<td>86 (19.5)</td>
</tr>
</tbody>
</table>

**Key:** AFB+: Acid Fast Bacilli smear positive, INH: Isoniazid, RIF: Rifampicin, MDR: Multidrug resistance

The mono-resistance as tested by GenoType® MTBDRplus assay was 2.7%, 2.9% in sputum samples from INH and RIF respectively. The mono-resistance from culture positive was 19.5% and 20.5% for INH and RIF respectively.
and RIF respectively. The results of the present study revealed that 7.4% (115/1548) are MDR-TB (Table 1). Out of 614 conventional DST processed, 5 (0.8%) were contaminated and the DST could not be ascertained hence there was no DST result. Although DST results were not available, these samples gave an interpretable Isoniazid and Rifampicin results by GenoType® MTBDRplus assay. Of which, 2 (0.3%) and 1 (0.2%) were resistant to Isoniazid and Rifampicin respectively. While, 3 (0.5%) and 4 (0.6%) were susceptible to Isoniazid and Rifampicin respectively (Table 2).

### Table 2: GenoType® MTBDRplus assay compared with conventional Drug Susceptibility Testing

<table>
<thead>
<tr>
<th>Growth outcome</th>
<th>Conventional Drug Susceptibility Testing</th>
<th>GenoType® MTBDRplus</th>
<th>Positive growth n(%)</th>
<th>DST contaminated n(%)</th>
<th>Total n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>Susceptible</td>
<td>495 (80.6)</td>
<td>3 (0.5)</td>
<td>498</td>
<td></td>
</tr>
<tr>
<td>Resist</td>
<td>Resistant</td>
<td>114 (18.5)</td>
<td>2 (0.3)</td>
<td>116</td>
<td></td>
</tr>
<tr>
<td>Rifampicin</td>
<td>Susceptible</td>
<td>487 (79.3)</td>
<td>4 (0.6)</td>
<td>491</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Resistant</td>
<td>122 (19.8)</td>
<td>1 (0.2)</td>
<td>123</td>
<td></td>
</tr>
</tbody>
</table>

### Discussion

The Mycobacteriology Section Laboratory within the Rwanda National Reference Laboratory is the referral laboratory for culture of Mycobacteria and DST for TB diagnosis and patients follow-up in Rwanda. The laboratory is receiving approximately 20 to 30 sputum samples for primary culture and DST daily. Even though GenoType® MTBDRplus assay is considered as the most effective, reliable and fast line probe assay used for rapid detection of pulmonary TB and MDR-TB from AFB smear positive and MTB isolates [7], evaluating the performance of the new laboratory tool is a prerequisite before its implementation in the routine testing in our setting.

The present study assessed the performance characteristics including sensitivity, specificity, Positive Predictive Values (PPV) and Negative Predictive Values (NPV) of the GenoType® MTBDRplus assay for the detection of resistance to INH, RIF and MDR-TB from sputum specimens or isolates from primary culture. The GenoType® MTBDRplus assay was applied in parallel with conventional isolation and direct susceptibility testing procedures routinely used in mycobacteriology laboratories on egg-based L-J medium [13].

The current study presents the results of 1548 suspected MDR-TB patients from all health facilities in Rwanda enrolled in our study. At the same time, DST using conventional method “the proportional method”, taken as gold standard, was applied. GenoType® MTBDRplus assay was performed directly on sputum samples whose smear was positive and culture positive isolates. In total, 1548 patients were enrolled in the present study, from which 1106 (71.4%) were sputum samples and 442 (28.6%) were isolates from primary cultures. The detection rate in isolates (99.3%) compared to the detection performed from sputum (15.8%) was statistical significant (p<0.0001) if the GenoType® MTBDRplus assay was applied directly on isolates. We observed at the same time a high number of MDR-TB patients (19.5%) detected from isolates while there was a relative low number of MDR-TB (2.6%) detected from smear positive sputum (Table 1). However, the results of the present study show a slight low number of MDR-TB (7.4%) patients compared to the previous study conducted in Rwanda (9.4%) from previous treated patients [14].

Resistance patterns studied were monoresistance to isoniazid and rifampicin as well as multi-drug resistance profiles from either fresh sputum samples or culture positive isolates. The
GenoType MTBDRplus assay showed a good performance in detection of both INH and RIF mono-resistance. However, there was no statistical significant difference between detection of INH monoresistance (2.7%) and RIF monoresistance (2.9%) from sputum samples smear positive, or between detection of INH monoresistance (19.5%) and RIF monoresistance (20.5%) from isolates (p=0.52). Moreover, the difference in detection of monoresistance for INH and RIF monoresistance was statistically significant from isolates culture positive compared to that from fresh sputum specimens smear positive (p<0.05). When the test was performed directly on sputum, the yield was not as good as when it was performed on isolates. One observation was that the GenoType MTBDRplus assay performed well on specimens whose primary or DST culture was contaminated what constitutes an advantage of the molecular test over the phenotypic DST. One RIF and two INH resistant results could be missed out by conventional DST but were revealed by the GenoType MTBDRplus test (Table 2). These results sound the same with those found elsewhere in which contaminated culture GenoType MTBDRplus assay gave an interpretable results [9]. Misdiagnosing TB and MDR-TB can lead to late treatment, thus spreading the infection in the entire population.

Performance of GenoType MTBDRplus sensitivity, specificity, positive predictive values and negative predictive values

To assess the performance characteristics of GenoType MTBDRplus test, the sensitivity, specificity, PPV and NPV were calculated from samples for which both GenoType MTBDRplus and conventional DST tests were performed as well. Our findings show that GenoType MTBDRplus assay has a good sensitivity and specificity as performance characteristics. Its sensitivity to detect Isoniazid resistance is 94.8% (95% CI 79.8-99.3), and Rifampicin 91.7% (95% CI 77.5-98.2). The sensitivity for both INH and RIF was 93.8% (95% CI 79.2-99.2%) for MDR TB. The specificity to detect resistance patterns was 99.3% (95% CI 96.2-100.0) for Isoniazid, 98.6% (95% CI 94.9-99.8) for Rifampicin and for the detection of MDR-TB it was 99.0% (95% CI 96.2-100.0) for both INH and RIF resistance. The test has a quite high specificity compared to its sensitivity in detecting INH, Rif resistance and MDR-TB cases (Table 3). The low sensitivity to detect INH and Rif resistance patterns could be explained by the lack of some probes to detect all alleles conferring any given mutation and if these all probes are included, it could improve the detection of all INH and RIF resistance patterns. Results from several studies conducted elsewhere in the world to evaluate the performance of GenoType MTBDRplus assay, have reported similar results to our findings. A meta-analysis to validate GenoType MTBDRplus assays for the diagnosis of Multidrug-Resistant Tuberculosis showed 98%, 89% of sensitivity and specificity respectively [8]. Others studies presented similar results with a slight high specificity (100%) for RIF resistance in South Africa. Moreover, similar sensitivity was documented in these studies respectively as follow: 94.2% and 98.9% for INH respectively in Thailand and South Africa. In Thailand the sensitivity to detect INH, Rif resistance and MDR-TB was 95.3%, 100%, and 94.4% respectively [7,9]. However, when compared to what has been found in other studies, our assessment showed that the GenoType MTBDRplus assay in our setting did not achieve 100% specificity to detect MDR-TB cases.

Compared to our findings, a study conducted in South Vietnam by Hueyen M.N. et al, has found that by conventional DST, 55 strains were classified as MDR-TB, four strains were rifampicin mono-resistant and 52 strains were susceptible to all first-line drugs. The sensitivity of the GenoType MTBDRplus assay was 93.1% for rifampicin, 92.6% for isoniazid and 88.9% for the combination of both; its specificity was 100% [15]. However, the specificity of GenoType MTBDRplus assay to detect MDR-TB, in our study, was lower than that found in other studies conducted elsewhere in the world [7,9,15].

The positive predictive value (PPV) of GenoType MTBDRplus assay is 96.7% (95% CI: 93.8-99.6) while its negative predictive value (NPV) is 98.6% (95% CI: 94.9-99.8) for Isoniazid. The pooled PPV and NPV for multidrug resistance (MDR) are 96.8% (95% CI: 93.9-99.8) and 98.6% (95% CI: 94.9-99.8) respectively. The lower NPV and PPV could be explained by low TB prevalence in our setting where the estimated TB incidence rates in Rwanda which is lower than the Global and AFRO Regional average, 86 incident TB cases -new and relapse- per 100,000 inhabitants in Rwanda in 2012 vs. 122 and 255 respectively at global and AFRO Region level [16].

Turnaround time

The turnaround time (TAT) evaluated included only the time between inoculation of the test sample and the availability of conventional DST results or the date of GenoType MTBDRplus results from the computerized National Reference Laboratory database. The additional time including the date of sample collection, the period of storage and transport were not included in the calculation of TAT. We considered the date between the inoculation of the test and the availability of the results. In the routine testing for laboratory TB diagnosis, using solid culture and indirect susceptibility testing, the total turnaround time takes weeks and even months in many laboratories [17]. In the present evaluation, the difference in TAT is statistical significant when applying GenoType MTBDRplus assay on fresh sputum as well as on clinical isolates (p<0.05). The reduction of TAT confers to the GenoType MTBDRplus assay the ability of rapid TB and MDR-TB diagnosis, thus initiation early TB treatment and MDR-TB case management is made possible with the new test method. Thus, GenoType MTBDRplus assay can serve as an early guidance of MDR-TB treatment and case management. The GenoType MTBDRplus assay is considered as alternative tool to diagnose TB and MDR-TB in few days rather than DST performed on L-J solid medium which takes several weeks to months. The present performance assessment ensured that GenoType MTBDRplus assay can be used for early TB and MDR-TB diagnosis so early appropriate treatment can be instituted.

Conclusions

GenoType MTBDRplus assay is a rapid and reliable test to be implemented in Rwanda. Considering the short turnaround time, ease of use, its accuracy, specificity and low infrastructure requirements, the GenoType MTBDRplus assay is an alternative tool for routine testing in Rwanda of MDR-TB detection in order to institute early treatment. Furthermore, monoresistance of multidrug resistance were neither associated with drug resistance nor type of specimen analyzed.

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