Comparison of performance of two DNA line probe assays for rapid detection of multidrug-resistant isolates of Mycobacterium tuberculosis

Suhail Ahmad*, Noura M Al-Mutairi & Eiman Mokaddas
Department of Microbiology, Faculty of Medicine, Kuwait University, P.O. Box 24923, Safat, 13110, Kuwait

Received 18 December 2008

Infections with multidrug-resistant (resistant at least to rifampicin, RIF and isoniazid, INH) strains of Mycobacterium tuberculosis (MDR-TB) are associated with high case fatality rates. Rapid identification of MDR-TB strains is important for early institution of appropriate therapy. Two DNA line probe assays, GenoType MTBDR (GT-MTBDR) and INNO-LiPA Rif. TB (INNO-LiPA) were compared for their abilities to detect resistance to INH and RIF in 80 M. tuberculosis isolates. The test results were compared to those obtained by conventional drug susceptibility testing (DST), DNA sequencing and/or PCR-restriction fragment length polymorphism (RFLP) analysis of regions of interest of M. tuberculosis genome. Compared to the DST and \textit{katG} codon 315 PCR-RFLP results, GT-MTBDR test results were concordant for INH resistance for 63 of 80 (78.7%) isolates. For RIF resistance, GT-MTBDR and INNO-LiPA test results were concordant with DST for 74 of 80 (92.5%) and 76 of 80 (95%) strains, respectively. The GT-MTBDR test results correlated with sequencing results for 77 of 80 (96.2%) while INNO-LiPA results for 79 of 80 (98.7%) isolates. Both the tests are useful for rapid detection of MDR-TB strains, however, GT-MTBDR assay offers the advantage of detecting the resistance to both INH and RIF simultaneously when MDR-TB is suspected.

**Keywords:** GenoType MTBDR, INNO-LiPA Rif. TB, Line probe assays, Multidrug resistance, Mycobacterium tuberculosis, resistance

\textit{Mycobacterium tuberculosis} remains an important cause of death from an infectious agent, killing nearly two million people worldwide every year\textsuperscript{1,2}. Prevention and control of tuberculosis (TB) is hampered by the expanding human immunodeficiency virus (HIV) infection and its association with active disease and increasing resistance of \textit{M. tuberculosis} strains to the most effective (first-line) anti-TB drugs\textsuperscript{3,4}. An important measure of the problem of drug-resistant TB in any country is the number of new cases that are resistant to both rifampicin (RIF) and isoniazid (INH) (defined as multidrug-resistant TB, MDR-TB) since MDR-TB is difficult to treat and often results in relapse or treatment failure\textsuperscript{4,6}. Prevalence of MDR-TB has been reported to vary from 0% to ~10% among different countries around the world\textsuperscript{4}. Rapid identification of MDR-TB strains is crucial for initiation of effective chemotherapy to ensure successful treatment of the patient and for infection control measures to arrest further transmission of these strains.

Development of drug resistance in \textit{M. tuberculosis} strains is due to random genetic mutations in specific genes conferring resistance and MDR-TB strains evolve due to sequential accumulation of these mutations\textsuperscript{6,7}. The resistance of \textit{M. tuberculosis} to RIF occurs infrequently and is mainly (in 90-95% of all RIF-resistant strains) due to mutations in an 81bp hot-spot region of the \textit{rpoB} gene, corresponding to codons 507 to 533 (\textit{Escherichia coli} numbering system) encoding β-subunit of RNA polymerase\textsuperscript{7,10}. Monoresistance to RIF is rare and a vast majority (>90%) of RIF-resistant strains are also resistant to INH\textsuperscript{4,7,11-13}. Thus, detection of resistance of \textit{M. tuberculosis} to RIF is also regarded as a surrogate marker for MDR-TB\textsuperscript{3,11,14}. On the contrary, resistance of \textit{M. tuberculosis} strains to INH develops more frequently and arises due to mutations in several regions of multiple genes\textsuperscript{7,15}. However, mutations in \textit{katG} gene encoding catalase-peroxidase that is required to activate the prodrug INH to its active form occur more frequently and nearly 50 to 95% of INH-resistant strains worldwide have been reported to contain mutations in codon 315 of the \textit{katG} gene (\textit{katG315})\textsuperscript{7,15-20}.

\*Correspondent author
Telephone: 00965-498-6503; Fax: 00965-531-8454
E-mail: suhail_ah@hsc.edu.kw; suhail_ah2000@yahoo.com
Several molecular methods have been developed in recent years to detect mutations in \textit{rpoB} and \textit{katG} genes for RIF and INH resistance detection, including DNA sequencing, PCR-restriction fragment length polymorphism (RFLP) pattern analyses, multiplex allele specific PCR, line probe assays and analysis with DNA microarrays \cite{6,7,15}. Although DNA sequencing-based methods are considered the reference assays for the detection of mutations, they are often regarded as technically demanding and too cumbersome for routine use. Commercial line probe assays have been developed to allow the prediction of drug resistance in clinical \textit{M. tuberculosis} isolates within one working day \cite{21,25}. The INNO-LiPA Rif. TB (INNO-LiPA), a reverse hybridization-based line probe assay has previously been evaluated for detection of mutations conferring resistance to RIF in \textit{M. tuberculosis} isolates \cite{9,21,22}. The GenoType MTBDR (GT-MTBDR) test is based on the same general principle as the INNO-LiPA test but offers the advantage of detection of both \textit{rpoB} and \textit{katG} genes simultaneously and thus predicts resistance to both RIF and INH \cite{23,25}. Aim of this study was to compare performances of GT-MTBDR and INNO-LiPA tests for rapid detection of MDR among \textit{M. tuberculosis} strains isolated in Kuwait and Dubai. Line probe assay results have been compared with results obtained by conventional (phenotypic) drug susceptibility testing (DST) performed on each strain and data were obtained by DNA sequencing and/or PCR-RFLP pattern analysis of respective chromosomal regions of \textit{M. tuberculosis} genome.

Materials and Methods

\textit{M. tuberculosis} strains (72) obtained from 72 different patients at Kuwait National Tuberculosis Reference Laboratory (KNTRL) in Shuwaikh, Kuwait and 8 strains isolated from 8 different patients at Rashid Hospital, Dubai, United Arab Emirates were used in this study. Additionally, 19 repeat isolates recovered from 19 TB patients at KNTRL within 1 to 2 months of isolation of the first isolate were also analyzed. Isolation of mycobacterial isolates from clinical specimens was performed using the mycobacterial growth indicator tube 960 system (Becton Dickinson, Sparks, MD, USA) as described previously \cite{26}. Conventional identification of \textit{M. tuberculosis} isolates was performed by the NAP test \cite{27}. Molecular identification of the isolates as \textit{M. tuberculosis} isolates was carried out by a multiplex PCR assay that was performed as described earlier \cite{28}. The DST of clinical \textit{M. tuberculosis} isolates was performed using the BACTEC 460 TB system as reported earlier \cite{5,26}. Isolates were considered resistant to corresponding drug when bacterial growth occurred in the presence of RIF (2 μg/mL) or INH (0.1 μg/mL) or ethambutol (EMB, 2.5 μg/mL) or streptomycin (STR, 2 μg/mL). Isolates that were simultaneously resistant to RIF and INH with or without additional resistance to EMB and/or STR were defined as MDR-TB strains. Some of the clinical isolates were analyzed previously by the GT-MTBDR or INNO-LiPA assays \cite{29,30}. \textit{M. tuberculosis} reference strain H37Rv was used as a control in DST, line probe assays, DNA sequencing and PCR-RFLP analyses of respective chromosomal regions of \textit{M. tuberculosis} genome.

For PCR amplification, genomic DNA from \textit{M. tuberculosis} H37Rv and BACTEC liquid cultures was prepared by incorporating removal of PCR inhibitors as described earlier \cite{31}. Epidemiological linkage among MDR-TB strains was studied by genetic group analysis based on polymorphisms at \textit{katG} codon 463 (\textit{katG463}) and \textit{gyrA} codon 95 (\textit{gyrA95}) and by touchdown double-repetitive-element (DRE)-PCR. Presence of Arg463/Leu463 at \textit{katG463} was determined by PCR amplification of \textit{katG463} DNA region by using KatG1F and KatG1R primers followed by restriction digestion of amplicons with restriction endonuclease \textit{Nci I} to generate RFLP patterns as described earlier \cite{32}. Presence of Ser95/Thr95 at \textit{gyrA95} was also determined by PCR amplification of \textit{gyrA95} DNA region by using GYRA95F and GYRA95R primers followed by restriction digestion of amplicons with restriction endonuclease \textit{Ale I} to generate RFLP patterns as described earlier \cite{33}. Touchdown DRE-PCR for fingerprinting of MDR-TB isolates was performed by using outward primers (\textit{IS6110-5′R}, 5′-GGCTGAGGCTTCAGACGAG-3′; \textit{IS6110-3′F}, 5′-ACCCCCATCCCTTTCCAAGAAT-3′; \textit{PGRS-5′R}, 5′-TCCCCCGCGTGGCGTACAG-3′ and \textit{PGRS-3′F}, 5′-CTGGGAAACCGCCACGCAGT-3′) derived from the two repetitive elements \textit{IS6110} and poly GC rich sequences (PGRS) as described previously \cite{33}. \textit{M. tuberculosis} isolates belonging to different genetic groups and/or yielding unique patterns of DNA amplified fragments in DRE-PCR were considered as genotypically distinct strains.
GT-MTBDR assay (Hain Life Sciences, Nehren, Germany) was performed according to instructions supplied with the kit. Briefly, the 250bp region of \( rpoB \), 120bp region around \( katG315 \) and a 200bp 23S rRNA gene region specific for high G + C gram-positive bacteria were amplified by multiplex PCR. Biotinylated amplicons were denatured and hybridized with specific oligonucleotides immobilized on GT-MTBDR strips under strictly controlled conditions as recommended by the kit manufacturer. Addition of alkaline phosphatase-labeled streptavidin conjugate followed by incubation with chromogenic substrate (5-bromo-4-chloro 3-indolylphosphate-nitroblue tetrazolium) resulted in detection of hybridized amplicons as purple precipitate on GT-MTBDR strips.

GT-MTBDR assay results were interpreted as instructed by the kit manufacturer. Presence of \( M. \) tuberculosis DNA is detected with 2 probes (universal control and \( M. \) tuberculosis complex, MTC control). Amplification of \( rpoB \) gene fragment is detected by \( rpoB \) control probe while 5 partially overlapping \((rpoB\ WT1\ to\ rpoB\ WTS)\) probes hybridize to wild-type (WT) sequence in \( rpoB \) gene. Hybridization of WT probes is prevented (\( \Delta WT \)) by mutations in \( rpoB \) gene region covered by the corresponding probe. Additional probes (4); \( rpoB \) MUT1 (D516V), \( rpoB \) MUT2A (H526Y), \( rpoB \) MUT2B (H526D) and \( rpoB \) MUT3 (S531L) hybridize to mutant sequences of the 4 most commonly observed mutations. Similarly, amplification of \( katG315 \) region is detected by \( katG \) control probe while \( katG \) WT probe hybridizes to wild-type \( katG315 \) (\( katG315AGC \)). Reactivity of an amplified fragment with \( katG \) WT probe is prevented if a mutation is present at \( katG315 \). Additional probes (2); \( katG \) MUT1 (AGC315ACC, S315T) and \( katG \) MUT2 (AGC315ACA, S315T) hybridize to mutant sequences of the 2 most commonly observed mutations at \( katG315 \). When all of the wild-type probes give a positive signal and none of the mutant probes react, the \( M. \) tuberculosis isolate is considered as susceptible to RIF and INH (wild-type or susceptible pattern). When at least one negative signal (\( \Delta \)) is obtained with \( rpoB \) WT probes, the isolate is RIF-resistant. When resistance to RIF is due to one of the 4 most frequently observed mutations described above, a positive reaction is also obtained with an \( rpoB \) mutant probe. When a negative signal is obtained with the \( katG \) WT probe, the isolate is INH-resistant. When resistance to INH is due to the presence of most common mutations at \( katG315 \) described above, a positive reaction is also obtained with a \( katG \) mutant probe. Concomitant RIF and INH resistance pattern indicates MDR status of the isolate.

INNO-LiPA assay (Innogenetics N V, Ghent, Belgium) was also used according to the instructions supplied by the kit manufacturer. Briefly, the hot-spot region of the \( rpoB \) gene was amplified from \( M. \) tuberculosis isolates by PCR\(^9,21\). Biotinylated amplicons were hybridized with specific oligonucleotide probes immobilized on nitrocellulose paper strips provided with the kit under controlled conditions. After hybridization, alkaline phosphatase-labeled streptavidin was added and bound to any biotinylated hybrid previously formed. Incubation with substrate (5-bromo-4-chloro 3-indolylphosphate-nitroblue tetrazolium) resulted in purple precipitate on paper strips. INNO-LiPA assay results were interpreted as reported earlier\(^9\).

GT-MTBDR and INNO-LiPA test results for RIF resistance detection were confirmed by DNA sequencing of \( rpoB \) codons 462 to 591 including codons 509 to 533 of the hot-spot region. Amplification of genomic DNA containing hot-spot region of the \( rpoB \) gene (accession No. L27989) from \( M. \) tuberculosis isolates was performed by touchdown PCR with hot start as described earlier\(^31\) except that primers RPOHSF (5′-GACGACATCAGCATTTCG-GCAAC-3′) and RPOHSR (5′-GAACGGGTTGACCCCCCGGCTACA-3′) were used. DNA sequencing of 426bp amplicons was performed as described\(^35\) except that primer RPO4FS (5′-AAACCAGATCCGGGTTGCGATGTG-3′) or primer RPO4RS (5′-GCGTACACCGAGCCAGCGGCAAGCCGA-3′) was used and both strands were sequenced. DNA sequencing identified mutations as specific base changes at the respective \( rpoB \) codons.

GT-MTBDR test results for INH resistance detection were confirmed by amplification of \( katG315 \) DNA region by PCR followed by restriction digestion of the purified amplicons with \( Msp \) I and \( MspA1 \) I to generate RFLP patterns as described earlier\(^34\). Results of PCR-RFLP analyses were also confirmed by DNA sequencing of 355bp amplicons containing the \( katG315 \) DNA region for some randomly selected isolates. DNA sequencing was also performed as described earlier and identified mutations as specific base changes at \( katG315 \)\(^21,34\).

Sensitivity of GT-MTBDR and INNO-LiPA assays in detecting RIF-resistant, INH-resistant and MDR
Results

All the 80 clinical isolates analyzed in this study were identified as *M. tuberculosis* strains based on specific amplification of 2 DNA fragments of 473 and 235bp in multiplex PCR assay that distinguishes *M. tuberculosis* complex strains from non-tuberculous mycobacteria (data from 14 randomly selected isolates are shown in Fig. 1). Based on the results of the conventional DST by BACTEC 460 TB system, 30 of 80 isolates were susceptible to all first-line drugs (pansusceptible strains) while 14, 7, 10 and 19 isolates were resistant to RIF and INH; RIF, INH and STR, RIF, INH and EMB and RIF, INH, EMB and STR, respectively. Thus, 50 of the 80 isolates were MDR-TB strains.

None of the 30 RIF-susceptible isolates contained a mutation in the *rpoB* gene. Of the 50 isolates that were phenotypically resistant to RIF, DNA sequencing data showed that 47 (94%) isolates contained a mutation while the remaining three isolates contained wild-type sequences in the *rpoB* gene (Table 1). The mutation TCG531TTG (S531L) was most common (25 of 50, 50%) while CAC526TAC (H526Y), CAC526GAC (H526D) and GAC516GTC (D516V) mutations were detected in 1 of 50 (2%), 3 of 50 (6%) and 6 of 50 (12%) RIF-resistant strains, respectively. Other single point mutations were found in 10 RIF-resistant strains while two isolates contained dual mutations (D516E + S522L and D516G + H526Q) (Table 2). GT-MTBD and INNO-LiPA test results (data from one pansusceptible and seven randomly selected MDR *M. tuberculosis* isolates are shown in Fig. 2a and b, respectively) correlated with phenotypic DST for RIF for 74 of 80 (92.5%) and 76 of 80 (95%) isolates, respectively (Table 1). GT-MTBDR and INNO-LiPA test results were concordant with *rpoB* sequencing results for 77 of 80 (96.2%) and 79 of 80 (98.7%) isolates, respectively (Table 1). No mutation was detected in the 30 phenotypically RIF-susceptible isolates by both, the GT-MTBDR and INNO-LiPA tests. The most commonly observed mutations at codon 531, 526 and 516 (S531L, H526Y, H526D and D516V) that were found in 35 of 50 (70%) RIF-resistant isolates were accurately detected by the wild-type as well as mutant probes included in both, the GT-MTBDR test and INNO-LiPA assay (Table 2). Other less frequently observed single or dual mutations (H526R, H526Q, S522L, D516G, D516E, Q513K or Q513L) were only detected by the inability of the corresponding wild-type probes to react in both, the GT-MTBDR test and INNO-LiPA assay (Table 2). Three RIF-resistant isolates gave discrepant results by the two strip tests. One isolate with H526P

![Fig. 1—Representative agarose gel of multiplex PCR products from 14 randomly selected isolates (lanes 1-14) showing *M. tuberculosis*-specific amplification of 473 and 235bp fragments (→) of *oxyR* and *rpoB* genes, respectively. [Lane M-100bp DNA ladder and position of migration of 100 and 600bp fragments are marked]
and another one with L533P mutation were erroneously identified as RIF-susceptible by GT-MTBDR test while INNO-LiPA assay correctly identified these isolates as RIF-resistant. One isolate with insertion 514TTC mutation was identified as susceptible to RIF by both, the GT-MTBDR and INNO-LiPA tests (Table 2).

Of the 50 isolates that were phenotypically resistant to INH, PCR-RFLP analyses of katG315 DNA region and GT-MTBDR test showed that 33 (66%) isolates contained a mutation while the remaining 17 isolates contained wild-type katG315.

None of the 30 phenotypically documented INH-susceptible isolates contained a mutation at katG315 (Table 3). The GT-MTBDR test results correlated with phenotypic DST for INH for 63 of 80 (78.7%) isolates (Table 3). The GT-MTBDR test results were also concordant with PCR-RFLP analyses of katG315 DNA region for 63 of 80 (78.7%) isolates (Table 3). The INNO-LiPA assay does not include probes for the analysis of mutations at katG315 and thus does not detect INH resistance of Mycobacterium tuberculosis isolates.

The genetic group analysis and fingerprinting patterns obtained in DRE-PCR showed that majority of MDR-TB strains were unique strains and were not epidemiologically related. The repeat isolates recovered from 19 TB patients yielded the same resistance pattern and the same profiles in the two line probe assays as the parent isolate (data not shown).

Comparative results of phenotypic DST by BACTEC 460 TB system and genotypic testing by GT-MTBDR assay for both RIF and INH are presented in Table 4. Majority (30 of 50, 60%) of phenotypically documented MDR M. tuberculosis isolates were accurately detected by the GT-MTBDR assay while an additional 28% (14 of 50) and 6% (3 of 50) MDR-TB strains were detected as mono-resistant to RIF and INH, respectively. All the 30 strains susceptible to both, RIF and INH were accurately detected by GT-MTBDR assay while 6%
Table 4—Comparison of phenotypic BACTEC 460 TB system and GenoType MTBDR (GT-MTBDR) assay results for simultaneous detection of rifampicin (RIF) and isoniazid (INH) susceptibility among 80 M. tuberculosis isolates

<table>
<thead>
<tr>
<th>Susceptibility to rifampicin</th>
<th>Susceptibility to isoniazid</th>
<th>No. of isolates identified by BACTEC 460 TB</th>
<th>GT-MTBDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistant</td>
<td>Resistant</td>
<td>50</td>
<td>30</td>
</tr>
<tr>
<td>Resistant</td>
<td>Susceptible</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Susceptible</td>
<td>Resistant</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Susceptible</td>
<td>Susceptible</td>
<td>30</td>
<td>33</td>
</tr>
</tbody>
</table>

(3 of 50) of MDR-TB strains were erroneously detected as susceptible to both RIF and INH.

Discussion

For the susceptible M. tuberculosis strains, the GT-MTBDR and INNO-LiPA test results were 100% concordant with DST and rpoB sequencing for RIF resistance detection. Likewise, GT-MTBDR test results were also 100% concordant with DST and katG315 PCR-RFLP results for INH resistance detection. The 35 of 50 (70%) isolates containing S531L, H526Y, H526D and D516V mutations were correctly identified by the mutant probes of both, the GT-MTBDR and INNO-LiPA tests. Occurrence of S531L mutation in 50% (25 of 50) of MDR-TB strains is also consistent with the occurrence of this mutation in MDR isolates in other studies. Nine isolates containing one or more mutations within the rpoB gene were only detected as RIF-resistant by the inability of the corresponding rpoB WT probe to react in both, the GT-MTBDR and INNO-LiPA assay. Interestingly, 2 of these isolates contained D516G mutation (one isolate with D516G and another isolate with D516G in combination with H526Q) which was
not detected by the GT-MTBDR test in a previous study\textsuperscript{24}. However, 3 of 50 (6\%) MDR isolates carrying a mutation in the hot-spot region were erroneously detected as RIF-susceptible by one or both the tests. Consistent with previous reports, the isolate with an insertion mutation at codon 514 (insertion 514 TTC) was detected as RIF susceptible by both, the GTMTBDR and INNO-LiPA tests\textsuperscript{22,35,36}. On the contrary, one isolate each with H526P and L533P mutation were correctly identified as RIF-resistant by INNO-LiPA assay; however, the GT-MTBDR test scored these isolates as RIF-susceptible. Presence of L533P mutation was detected by the lack of a signal with \textit{rpoB} WT5 probe in two previous studies\textsuperscript{36,37} while isolates with H526P mutation have not been tested previously with GT-MTBDR test\textsuperscript{23,25,36,37}.

In contrast to INNO-LiPA test that only detects the resistance of \textit{M. tuberculosis} isolates to RIF, GT-MTBDR assay offers additional advantage of detection of INH-resistant MDR strains carrying \textit{katG}315 mutations\textsuperscript{23-25}. For INH resistance detection, GT-MTBDR test results were 100\% concordant with DST and \textit{katG}315 PCR-RFLP results for INH-susceptible \textit{M. tuberculosis} strains. Furthermore, rate of concordance of INH resistance detection among MDR \textit{M. tuberculosis} strains by GT-MTBDR test with DST and \textit{katG}315 PCR-RFLP results were found to be 66\% (33 of 50). Results of this study are in agreement with the detection of INH resistance status of nearly 60\% MDR strains in several studies\textsuperscript{25,36,37}. Other investigators have reported a higher sensitivity of GT-MTBDR test to detect INH resistance status of MDR isolates\textsuperscript{23,24}. However, MDR-TB strains in these studies were isolated from geographical locations that are known to have a higher prevalence of \textit{katG}315 mutation among INH-resistant strains\textsuperscript{10,19,23}.

Taken together, for RIF resistance detection, rates of concordance of GT-MTBDR and INNO-LiPA tests with DST were found to be 92.5\% and 95\%, respectively, and with \textit{rpoB} sequencing as 96.2\% and 98.7\%, respectively. Other investigators have also reported similar sensitivities of both GT-MTBDR and INNO-LiPA tests for the detection of RIF-resistant strains\textsuperscript{21,25,35,37}. Concomitant detection of INH-resistant status by GT-MTBDR test allowed accurate identification of 60\% (30 of 50) of MDR \textit{M. tuberculosis} isolates.

Both GT-MTBDR and INNO-LiPA tests are easy to perform with a turnaround time of nearly 8 hr, reproducible and interpretation of results is easy and straightforward. However, band sizes and their intensities were nearly always same in INNO-LiPA assay while in GT-MTBDR test, band sizes as well as their intensities varied slightly for different isolates. Other investigators have also reported similar differences in the performance of two line probe assays\textsuperscript{24,25}. Another limitation of these rapid tests is inclusion of only specific probes for detection of the 4 most commonly observed mutations (S531L, H526Y, H526D and D516V) at three codon positions that are found in hot-spot region of the \textit{rpoB} gene. Other mutations at these codon positions as well as all mutations at other positions within the hot-spot region are detected only by the absence of a signal with one of the wild-type probes\textsuperscript{9,21-25}. Thus, the possibility of some non-synonymous mutations within the hot-spot region leading to the absence of a signal with one of the wild-type probes exists and the isolate will be considered as RIF-resistant. However, these mutations occur extremely rarely and have not thus far compromised the performance of the two line probe assays for detection of RIF resistance\textsuperscript{7,21-25,35-38}.

In conclusion, both GT-MTBDR and INNO-LiPA line probe assays are useful for rapid screening of \textit{M. tuberculosis} strains isolated from TB patients suspected of having MDR-TB. The INNO-LiPA assay detects MDR status only by virtue of detection of resistance to RIF which is generally regarded as a surrogate marker of MDR-TB. The GT-MTBDR test offers additional advantage of simultaneous detection of resistance to both RIF and INH. However, both assays fail to detect all resistant strains and the test results should always be confirmed by conventional DST results.

Acknowledgement

We thank Dr Esther Fares, Rashid Hospital, Dubai for providing some of the \textit{M. tuberculosis} isolates. This study was supported by Research Administration grant YM 03/06 and the College of Graduate Studies, Kuwait University.

References


