Evaluation of rapid diagnostic tests and assessment of risk factors in drug-resistant pulmonary tuberculosis

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ABSTRACT

Background: Early diagnosis and treatment of drug-resistant tuberculosis (TB) is crucial to halt the spread of drug resistance in the community. Aim: The aim of the study was to compare rapid diagnostic tests (GeneXpert and line probe assay, LPA) with conventional liquid culture for the diagnosis of drug-resistant TB and to assess the risk factors for it. Method: This cross-sectional study recruited 229 multidrug-resistant TB suspects who were sputum smear positive. They were evaluated by the rapid diagnostic tests and sensitivity, specificity, positive predictive value and negative predictive value were calculated for drug resistance detection as compared to liquid culture drug susceptibility testing. The risk factors for the development of drug resistance were also assessed and the P value of < 0.05 was considered significant. Results: In the final comparison, 193 samples were included. The sensitivity and specificity of GeneXpert for detection of drug resistance (rifampicin) was 100% (95% confidence interval, CI: 88.8–100%) and 99.4% (95% CI: 96.6–99.9%), respectively. Whereas sensitivity and specificity of LPA was 94.3% (95% CI: 80.8–99.3%) and 100% (95% CI: 97.7–100%), respectively. Only three discordant samples were observed. Defaulting to antitubercular therapy, contact with resistant TB, and disseminated disease were found to be significant risk factors for the development of drug-resistant TB with high statistical significance ($P$ value < 0.05). Conclusion: Both rapid diagnostic tests have very high sensitivity and specificity for detection of drug resistance in sputum smear positive with the advantage of short turn-around time. Defaulting to antitubercular therapy, contact with resistant TB, and disseminated disease are significant risk factors for drug resistance.

Keywords: GeneXpert, line probe assay, liquid culture, multidrug resistant tuberculosis

Introduction

Multidrug-resistant tuberculosis (MDR-TB) is a global challenge and early diagnosis and treatment are pivotal to halt its spread, especially in a resource-limited setting like ours where it has the highest incidence. MDR-TB accounted for 5,58,000 cases globally in the year 2017, out of this India accounted for 24% of the cases, which is highest in the world. The Global TB report, 2017 estimates that MDR-TB occurs in 3.5% of newly diagnosed cases and in 18% of re-treatment cases.¹,²

The conventional method for diagnosis of MDR-TB traditionally has been phenotypic drug susceptibility testing (DST) by solid ( Löwenstein–Jensen medium, LJ medium) or liquid culture (MGIT, Mycobacterium growth indicator tube). Although these tests are still considered “gold standard” for diagnosis of MDR-TB, they are limited by high contamination rates, the requirement of specialized laboratories, trained personnel, and high cost.³,⁴

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most importantly long turn-around time (around 84 days for LJ medium and 42 days for liquid culture DST). All of these limitations preclude their widespread implementation in our health care system.\[10\]

In the last decade, WHO has endorsed rapid molecular diagnostic tests like Xpert MTB/RIF (GeneXpert, Cepheid, Sunnyvale, California) and GenoType MTBDR\(plus\) (Hain Life science, Nehren, Germany; line probe assay, LPA) which are based on detection of mutation associated with resistance to first-line antitubercular drugs (rifampicin and isoniazid) and have emerged rapidly and are being used widely. GeneXpert targets the \(rpoB\) gene, simultaneously detecting \(Mycobacterium\) tuberculosis (MTB) bacteria and mutations responsible for rifampicin resistance. Similarly, LPA detects mutations responsible for rifampicin resistance by targeting the \(rpoB\) gene, and additional targets two additional genes, the \(katG\) gene for high-level isoniazid (INH) resistance and \(inhA\) regulatory region gene for low-level of INH resistance, respectively.\[5\,6\,7\]

The main advantage of these tests is the rapid turn-around time of just 2 h for GeneXpert and about 2–5 days for the LPA test. Additionally, GeneXpert does not require highly trained staff to run the machine or interpret the results. This advantage of GeneXpert has made it possible to expand it to remote peripheral levels for MTB detection and DST. However, the accuracy and performance of these rapid tests in comparison to the gold standard test need to be evaluated, especially under programmatic conditions. Our study intended to evaluate this diagnostic aspect along with finding some additional risk factors for the development of resistance.

This study is important for primary care physicians as they are often the first-care providers of the TB patients. This sensitizes the urgent need for rapid diagnosis of drug-resistant TB and early referral for treatment to halt the spread of drug resistance in the community. The importance of awareness about the risk factors for spread of drug-resistant TB cannot be emphasized enough.

**Methods**

**Study characteristics and patient recruitment**

It was a cross-sectional study conducted from April 2016 to February 2018 in the Department of Medicine at All India Institute of Medical Sciences (AIIMS), New Delhi. The subjects who were more than 12 years of age and fulfilled the criteria of MDR-TB suspect as per revised national tuberculosis control program (RNTCP) were screened and those who were sputum smear positive by Ziehl–Neelsen (ZN) staining were recruited for the study. These MDR-TB suspect cases are Category 1 failure cases, sputum positive during follow-up cases, MDR-TB contacts, previously treated pulmonary TB cases, and HIV-TB co-infected cases. The patients were recruited from chest clinics under intermediate reference laboratory (IRL, Department of Medicine), medicine out-patient department, Infectious Disease Clinic, Chest Clinic and DOTS center at AIIMS, New Delhi.

A thorough case history was obtained along with general and systemic examination and record of other relevant information like history and family history of TB, high-risk behavior, socioeconomic and occupational status, etc. All were noted. All baseline investigations like hemoglobin, liver and kidney function tests, blood sugar, and chest x-ray of the recruited patients were done and noted on a pre-designed proforma.

**Sample collection and diagnostic tests**

Two sputum samples were collected in a 50 ml wide-mouthed sterile falcon tube, as per RNTCP guidelines. One spot and one early morning sample were taken. The sputum specimens were handled in class IIA biosafety cabinet in the bio-safety level-3 (BSL-3) laboratory at IRL, AIIMS, New Delhi. Both sputum samples were subjected to ZN staining by standard protocol. The sputum positive samples were subjected to rapid molecular tests; GeneXpert and LPA along with MGIT culture and DST. All tests were performed simultaneously. The results of all three tests were noted and any discordant result noted was subjected to gene sequencing.

**GeneXpert**

It was done according to standard protocols as advised by the manufacturer, Cepheid, Sunnyvale, California, USA. The XpertMTB/RIF assay targets the 81bp rifampicin resistance determining region of the \(rpoB\) gene by five molecular probes named from A to E and simultaneously detects MTB bacterium without any cross-reactivity from other mycobacterial species or other bacteria. Turn-around time of GeneXpert is about 1 h 45 min.\[5\,6\,7\]

**Line probe assay**

LPA was done by commercially available LPA, GenoTypeMTBDR\(plus\) (Hain Life science, Nehren, Germany). After sputum decontamination and processing, the test was done according to protocols mentioned in the user manual of the test. The whole procedure is divided into three steps: (i) DNA extraction from the clinical specimen or cultured material, (ii) a multiplex amplification with biotinylated primers, and (iii) reverse hybridization. Turn-around time for the LPA test was around 48–72 h.\[10\]

**MGIT liquid culture and DST**

The de-contaminated and processed sputum sample was inoculated in MGIT liquid culture tubes. These tubes were placed in the BACTEC MGIT 960 instrument, where they were incubated at 37°C and monitored for the detection of growth. Any growth of mycobacteria increases the fluorescence which is captured by a fluorescent dye. DST was performed based on the same principle. Two MGIT tubes were inoculated with the test culture. A known concentration of the test drug was added to one of the MGIT tubes, and growth was compared with the MGIT tube without the drug (growth control). If the test drug was active against the isolated mycobacteria, it would inhibit the growth and thus there was suppression of fluorescence while the growth control grew uninhibited and had increasing fluorescence. Growth was monitored by the BACTEC 960 instrument which...
automatically interpreted the results as susceptible or resistant. All the tests were done in the BSL-3 lab, IRL, Department of Medicine, AIIMS, New Delhi, under strict precautions.10

### Data analysis

The patient’s data were recorded in a pre-designed proforma and entered in the Microsoft Excel sheet. Then, a descriptive analysis was performed. Categorical variables were expressed as numbers/frequency (percentages). The quantitative variables were expressed as mean and standard deviation, in case of skewed data, the median (minimum–maximum) was used. Statistical analysis was performed by STATA 14.0 statistical software. Sensitivity, specificity, positive and negative predictive values (PPV and NPV) and concordance and discordance rates were calculated using standard formulas after making 2 × 2 tables for all the test results and 95% confidence interval for each of them was calculated. Pearson Chi-square test and Fisher’s exact test was used to test the significance of differences observed between drug-resistant and drug-sensitive TB patients.

### Results

A total of 271 patients fulfilling criteria for MDR-TB suspects were screened with two sputum samples (spot and morning). Out of 271 patients, around 42 were found to be sputum acid fast bacilli (AFB) negative by ZN staining and were excluded from the study, rest 229 patients who were found to have sputum AFB positive were included in the study [Figure 1]. The clinical and laboratory features of the study subjects are mentioned in Tables 1 and 2.

#### MGIT liquid culture and DST results

Out of the 229 sputum positive samples, 196 (85.6%) were found to be culture positive, 29 (12.7%) were negative, 7 samples got

| Screening          | Excluded          | Recruited                  |
|--------------------|-------------------|----------------------------|
| Sputum microscopy  | Excluded          | ZN stain AFB+ (229)        |
| (2 samples)        |                   |                            |
| GeneXpert (229)    |                   | MGIT liquid culture (229)  |
| Line probe assay (229) |               | Culture negative - 29 Contaminated culture-4 Contaminated DST-3 |
| MGIT liquid culture (229) |           |                            |
| (n=229)            | RIF resistant-35  | DST (n=193)                |
| RIF sensitive-194  |                   | RIF & INH sensitive-156    |
|                    |                   | RIF & INH resistant-28     |
|                    |                   | INH mono-resistant-6       |
|                    |                   | RIF mono-resistant-3       |
| Gene sequencing of discordant samples (Total discordant result-3) | | |

Figure 1: Showing work-flow of the study; MDR-TB, multidrug resistant tuberculosis; ZN, Ziehl–Neelsen; AFB, acid fast bacilli; MGIT, mycobacteria growth indicator tube; DST, drug susceptibility testing; RIF, rifampicin; INH, isoniazid
Table 1: Clinical features of study population (n=229)

| Clinical features                                      | Numbers (percentages) |
|--------------------------------------------------------|------------------------|
| Compliance to antitubercular therapy - no. (%)         |                        |
| Defaulter                                              | 31 (13.5)              |
| Nondefaulter                                           | 198 (86.5)             |
| MDR-TB suspect criteria - no. (%)                      |                        |
| Failure                                                | 12 (5.2)               |
| Sputum positive at 4 months                            | 4 (1.7)                |
| MDR-TB contact                                         | 16 (7)                 |
| Previously treated                                     | 118 (51.5)             |
| Any follow-up positive                                 | 90 (39.3)              |
| HIV-TB co-infected                                     | 3 (1.3)                |
| Presenting complaints - no. (%)                        |                        |
| Productive cough                                       | 229 (100)              |
| Fever                                                  | 220 (96)               |
| Hemoptysis                                             | 126 (55)               |
| Weight loss                                            | 200 (87.3)             |
| Night sweats                                           | 45 (19.7)              |
| Shortness of breath                                    | 95 (41.4)              |
| History of tuberculosis - no. (%)                      |                        |
| No history                                             | 79 (34.5)              |
| Once                                                   | 130 (56.7)             |
| More than once                                         | 20 (8.7)               |
| History of MDR-TB contact - no. (%)                    |                        |
| Present                                                | 16 (7)                 |
| Absent                                                 | 213 (93)               |
| Physical findings- no. (%)                             |                        |
| Pallor                                                 | 94 (41)                |
| Lymphadenopathy                                        | 16 (7)                 |
| Clubbing                                               | 5 (2.2)                |
| Signs of Vitamin deficiency                            | 16 (7)                 |
| Abnormal chest exam                                    | 229 (100)              |
| Ascites                                                | 3 (1.3)                |
| Hepatosplenomegaly                                     | 4 (1.7)                |

Table 2: Laboratory investigations (n=229)

| Investigations                        | Values (SD/range/percentages) |
|---------------------------------------|------------------------------|
| Hemoglobin [g/dl]                     | 9.9±1.5                      |
| Urea [mg/dl]                          | 26.5±6.9                     |
| Creatinine [mg/dl]                    | 0.5 (0.2-2.3)                |
| Total bilirubin [mg/dl]               | 0.6 (0.2-3.2)                |
| AST (IU)                              | 32±11.4                      |
| ALT (IU)                              | 26±10.3                      |
| RBS (mg/dl)                           | 119.4±33.6                   |
| Chest X-ray findings - no. (%)        |                              |
| Cavity                                | 44 (19.2)                    |
| Upper lobe consolidation              | 132 (57.6)                   |
| Bilateral infiltrates                 | 86 (37.5)                    |
| Milary shadows                        | 12 (5.2)                     |
| Hilar lymphadenopathy                 | 15 (6.5)                     |
| Extensive fibrosis                    | 38 (16.6)                    |
| Pleural effusion                      | 13 (5.7)                     |

Results of GeneXpert test

GeneXpert detected 35/229 (15.3%) as rifampicin resistant of the total samples. Out of the culture-positive samples (193), GeneXpert detected 32/193 (16.6%) as rifampicin resistant. When compared to MGIT liquid DST for detection of rifampicin resistance, it detected accurately all samples found rifampicin resistant on MGIT liquid DST except one discordant sample which it showed as resistant and was found to be sensitive on MGIT DST [Table 3a]. The sensitivity and specificity of GeneXpert for detection of drug resistance (rifampicin resistance) was 100% (95% confidence interval, CI: 88.8–100%) and 99.4% (95% CI: 96.6–99.9%), respectively. Similarly, PPV and NPV of GeneXpert for rifampicin-resistant detection was 96.9% (95% CI: 81.4–99.5%) and 100%, respectively. Genetic sequencing of the discordant sample revealed a mutation in the rpoB gene thereby proving it to be resistant.

Results of LPA test

LPA detected a total 39/229 (17%) samples as drug-resistant, of which 30/229 (13.1%) were resistant to both rifampicin and isoniazid (MDR), 4/229 (1.7%) were rifampicin mono-resistant samples and 5/229 (2.2%) were isoniazid mono-resistant. Out of the culture-positive samples (193), LPA detected 35/193 (18.1%) as drug-resistant, of which 28/193 (14.5%) were resistant to both rifampicin and isoniazid, 3/193 (1.5%) were rifampicin mono-resistant and 4/193 (2%) were isoniazid mono-resistant. When compared to MGIT liquid DST for detection of drug resistance, LPA accurately detected all samples resistant on MGIT liquid DST but failed to detect two samples of isoniazid mono-resistant and showed them as sensitive [Table 3b]. Sensitivity and specificity for DR-TB detection was found to be 94.3% (95% CI: 80.8–99.3) and 100% (95% CI: 97.7–100), respectively. Similarly, the PPV and NPV of LPA for drug-resistant detection was found to be 100% and 98.7% (95% CI: 95.3–99.7), respectively.

There was one discordant result between LPA and GeneXpert [concordance rate – 99.6%] [Table 3e]. Whereas, there were two discordant samples observed between LPA and MGIT DST and both were for isoniazid mono-resistance (concordance rate – 98.9%). These false-negative samples were further tested by full gene sequencing of inhA and katG genes for detecting any mutation which LPA may have missed, but sequencing did not show any mutation in the above-mentioned genes. So, the likely cause of resistance can be other less commonly mutated genes like abpC-avxyR, kasA, rhlA, iniABC, etc.

Risk factors associated with drug-resistant TB

We also evaluated the factors associated with DR-TB in our study [Table 4]. Defaulting to antitubercular therapy (ATT) were compared with GeneXpert and LPA. MGIT liquid DST detected 37/193 (19.2%) samples as drug-resistant, of which 28/193 (14.5%) were resistant to both INH and RIF (MDR), 3/193 (1.5%) were rifampicin mono-resistant and 6/193 (3.1%) were isoniazid mono-resistant cases.

contaminated (4 during growth and 3 samples during DST). So, after eliminating these contaminated samples, a total of 193 samples with valid DST results were taken into account and...
is considered a strong risk factor for the development of DR-TB. In our study, 35.5% of patients who had history of defaulting to ATT (i.e., who left antitubercular treatment consecutively for more than 2 months after starting treatment, according to RNTCP) developed drug-resistant TB, as compared to 15.7% patients who had no history of defaulting to ATT, the values reached statistical significance (*P* value: 0.007). Drug-resistant TB was more likely to be associated with disseminated disease, around 34.1% patients who had disseminated disease had drug-resistant TB, as compared to localized pulmonary disease in which only 14.9% patients had drug-resistant TB, the difference observed was statistically significant (*P* value: 0.0038). Contact with a known MDR-TB case also came across as a strong risk factor of the development of MDR-TB. Around 62.5% patients who were exposed to MDR-TB case developed drug-resistant TB as compared to only 15% patients who developed drug-resistant TB had no contact with MDR-TB case; the values reached a high level of statistical significance (*P* value: 0.00009). Other factors studied like the history of TB and socioeconomic class although associated but didn’t reach any statistical significance.

**Discussion**

India is a country with the highest burden of drug-resistant TB in the world. There is an urgent need to tackle the spread of drug resistance in the community. Early diagnosis and treatment halts the spread of drug-resistant bacilli in the community but the current conventional diagnostic methods have long turn-around time and also require specific lab facilities. The present study was done to compare two rapid molecular diagnostic tests for the diagnosis of drug resistance with the conventional gold standard method i.e., MGIT liquid culture DST. The sensitivity and specificity of GeneXpert for rifampicin-resistant detection in sputum positive MDR-TB suspects was found to be almost similar (sensitivity and specificity 100% and 99.4%, respectively) to MGIT DST. GeneXpert can only determine resistant to rifampicin (not to isoniazid) and for operational purposes,

| Table 3: Comparative evaluation of all the tests |
|-----------------------------------------------|
| (a) Comparative evaluation of GeneXpert and MGIT liquid DST |
| GeneXpert                                      | MGIT liquid DST |
|                                               | RIF-r/INH-r     | RIF-r/INH-s     | RIF-s/INH-r | RIF-s/INH-s | Negative | Contaminated |
| RIF-r                                         | 28              | 3               | 0           | 1           | 1        | 2            |
| RIF-s                                         | 0               | 0               | 6           | 155         | 28       | 5            |
| Negative                                      | 0               | 0               | 0           | 0           | 0        | 0            |

| (b) Comparative evaluation of LPA and MGIT liquid DST |
|-------------------------------------------------------|
| LPA                                                   | MGIT liquid DST |
|                                                     | RIF-r/INH-r   | RIF-r/INH-s   | RIF-s/INH-r | RIF-s/INH-s | Negative | Contaminated |
| RIF-r/INH-r                                          | 28            | 0             | 0           | 0           | 1        | 1            |
| RIF-r/INH-s                                          | 0             | 3             | 0           | 0           | 0        | 1            |
| RIF-s/INH-r                                          | 0             | 0             | 4           | 0           | 1        | 0            |
| RIF-s/INH-s                                          | 0             | 0             | 2           | 156         | 27       | 5            |
| Negative                                             | 0             | 0             | 0           | 0           | 0        | 0            |

| (c) Comparative evaluation of LPA and GeneXpert       |
|-------------------------------------------------------|
| GeneXpert                                            | Line probe assay |
|                                                     | RIF-r/INH-r   | RIF-r/INH-s   | RIF-s/INH-r | RIF-s/INH-s | Negative |
| RIF-r                                                 | 30            | 4             | 0           | 1           | 0        |
| RIF-s                                                 | 0             | 0             | 5           | 189         | 0        |
| Negative                                              | 0             | 0             | 0           | 0           | 0        |

| Table 4: Factors associated with drug-resistant TB   |
|------------------------------------------------------|
| Condition                                           | Drug-resistant TB *(n=41)* | Drug-sensitive TB *(n=187)* | *P* (significant: <0.05) |
| Defaulters                                          | 11 (35.5%)               | 20 (64.5%)                 | 0.0079                  |
| Nondefaulters                                       | 31 (15.7%)               | 167 (84.3%)                |                          |
| History of TB                                       | 32 (21.3%)               | 118 (78.7%)                | 0.1069                  |
| History of TB                                       | 10 (12.6%)               | 69 (87.4%)                 |                          |
| Socio-economic class (<10 score)                    | 27 (19.7%)               | 110 (80.3%)                | 0.5141                  |
| >10 score                                           | 15 (16.3%)               | 77 (83.7%)                 |                          |
| Disseminated disease                                | 14 (34.1%)               | 27 (65.8%)                 | 0.0038                  |
| Localized Pulmonary disease                         | 28 (14.9%)               | 160 (85.1%)                |                          |
| MDR-TB contact                                      | 10 (62.5%)               | 6 (37.5%)                  | 0.00009                 |
| No-MDR TB contact                                   | 32 (15%)                 | 181 (85%)                  |                          |
rifampicin resistance is used as a surrogate marker for MDR-TB as cases of INH mono-resistance are very low. In our study, isoniazid mono-resistance was only 3.1% (by MGIT liquid DST) which is consistent with other similar studies.[10-14]

Similarly, for LPA, the sensitivity observed was 94.3% (95% CI: 80.8–99.3%) and specificity was 100% (95% CI: 97.7–100%). The sensitivity and specificity of GeneXpert and LPA for detection of drug-resistant TB is consistent with other previous studies in the literature which showed similar high sensitivity and specificity values with very low discordance rate. A study from Bangladesh by Aurin et al. in 2014 recruiting 300 patients compared GeneXpert and LPA with solid culture-based DST for MDR-TB detection and found sensitivity and specificity of GeneXpert and LPA as 99.5%, 97.7% and 99.5%, 98.8%, respectively. A total of only five discordant results were found in that study. Multiple other studies from other parts of the world like Rahman et al. (2016), Cantanzaro et al. (2015), Seuodi et al. (2011) similarly showed a very high sensitivity and specificity of these tests for resistance detection.[11-14]

More recently, a study from Kenya by Aricha et al. (2019) compared GeneXpert and LPA for detection of rifampicin mono-resistance and found that GeneXpert has just moderate agreement (sensitivity 62.5% and specificity 96.3%), but LPA has almost perfect agreement (sensitivity 90% and specificity 99.1%).[15]

In our study, the two rapid diagnostic tests (GeneXpert and LPA) showed high concordance in the detection of rifampicin resistance among themselves with only one discordant result.

The concordance rate for the detection of drug resistance between LPA and MGIT liquid DST was 98.9%. LPA did not show agreement with MGIT liquid DST in only two cases of isoniazid mono-resistance and GeneXpert showed one sample as resistant which was found to be sensitive on both LPA and MGIT DST. In our study, there were three discordant results obtained after the overall comparison of all tests. The likely cause of LPA showing discordance for INH resistance was due to other less common gene mutations, as unlike rifampicin in which almost all cases of resistance are due to a mutation in rpoB gene (96-98%), resistance to isoniazid is determined by genes other than inhA and katG in around 15% of patients. This was confirmed by genetic sequencing which did not show any mutation in inhA and katG genes.[16-18]

Among other factors studied between drug resistant and sensitive cases, drug-resistant TB is more likely to be associated with disseminated disease, a history of close contact with MDR case and defaulting to antitubercular drug therapy.[19,22] The present study emphasizes the fact that these rapid tests can be used for early detection of DR-TB as compared to the conventional culture-based tests so that timely treatment can be started and unnecessary cost and side-effects of MDR therapy can be avoided.

Our study investigated a very valid and important issue in TB which remains a major public health problem in our country, understandably a country with the highest global prevalence. The study was done with proper study design and appropriate data collection, with a broad vision to reduce the spread of drug resistance and reduce mortality from DR-TB by early diagnosis and treatment. It compared two most commonly used and WHO recommended rapid molecular tests (GeneXpert and LPA) and found that both of these tests can be used for accurate diagnosis of DR-TB in the community with significantly reduced time to accurately diagnose such cases.

Limitations

The major limitations of our study were a small sample size (which might have underestimated the actual discordant rate among these tests) and an inability to calculate cost-effectiveness due to logistic issues. So, perhaps future studies can be planned directed towards the calculation of cost-effectiveness of these tests. Also, one can assess disability-adjusted life years (DALYs) or work-days lost each year due to such illness and the extent to which these rapid tests reduce it as compared to the conventional method.

Conclusion

The study concludes that rapid molecular tests, GeneXpert, and LPA have high sensitivity and specificity for detection of DR-TB when compared with conventional liquid culture and DST with the additional advantage of having a very short turn-around time. LPA gives added advantage of detecting isoniazid mono-resistance but requires trained manpower and specialized laboratory. Future studies taking into account, cost-effectiveness and DALYs should be carried out for pragmatic evaluation of advantage of these rapid diagnostic tests.

In our country, each and every healthcare professional should be mindful of rapid diagnosis and treatment of drug-resistant TB and its risk factors to control this menace.

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Conflicts of interest
There are no conflicts of interest.
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