Original Article

Laboratory Cost Analysis of Conventional and Newer Molecular Tests for Diagnosis of Presumptive Multidrug-Resistant Tuberculosis Patients

Raj Narayan Yadav[1,2], Ajoy Kumar Verma[2], Gaurav Kaushik[1,3]

[1]Department of Medicine, All India Institute of Medical Sciences, New Delhi, India, [2]Department of Microbiology, National Institute of Tuberculosis and Respiratory Diseases, New Delhi, India, [3]School of Allied Health Sciences, Sharda University, Greater, Noida, India

Abstract

Introduction: Tuberculosis (TB) remains a deadliest infectious disease. Lack of rapid test with low cost is one of the important challenges to eradicate the TB. The objective of the study was to analyze the laboratory costs of conventional and newer molecular tests, for diagnosis of presumptive multidrug-resistant TB (MDR-TB) patients. **Methods:** A detailed laboratory cost of various conventional tests (Ziehl – Neelsen [ZN] microscopy, light-emitting diode-fluorescent microscopy [LED-FM], culture and drug susceptibility testing [DST] using solid Lowenstein–Jensen media and liquid media [BACTEC MGIT 960]) was compared with rapid methods (GenoType MTBDR*plus* line probe assay [LPA] and GeneXpert MTB/RIF assay). Laboratory cost was also calculated in terms of cost per TB and MDR-TB case detected by using different diagnostic scenarios. **Results:** Cost per test for ZN microscopy, LED-FM, LPA, GeneXpert MTB/RIF assay, solid culture plus DST, liquid culture plus DST was found as $2.5 (INR 156.8), $2.0 (INR128.9), $18.6 (INR1210), $13.8 (INR 895.2), $21.5 (INR 1396.6), and $29.1 (INR 1888.2), respectively. The laboratory cost for detecting TB and MDR-TB by diagnostic scenarios involving molecular DST was found to be less as compared to involving only conventional liquid culture-based test. **Conclusions:** The implementation of rapid molecular tests with selective use of liquid culture-based DST may be less in cost as compared to the use of culture-based DST alone, at high burden reference TB laboratory.

Keywords: Diagnosis, laboratory cost, multidrug-resistant tuberculosis, tuberculosis

Introduction

Tuberculosis (TB) remains one of the world's deadliest communicable diseases. About 10 million people became sick with TB, and 1.2 million deaths (among HIV-negative people) were reported from the disease in 2019.[1] Lack of rapid and accurate diagnostic tests with low cost is among the several challenges in controlling the TB disease. In developing countries, acid-fast bacillus (AFB) microscopy remains the keystone for the diagnosis of TB disease,[2] but its poor sensitivity is a major drawback. Solid and liquid culture methods for detection and drug-susceptibility testing (DST) of *Mycobacterium* TB (*Mtb*) are considered as the gold standard but these are time-consuming and require several weeks to months in providing the results. Furthermore, species identification contributes to delayed culture results. Unfortunately, these tests also require extensive infrastructure. To overcome these issues, the World Health Organization (WHO) has endorsed the use of new and advanced molecular techniques for the rapid detection of drug-resistant TB. These rapid diagnostic techniques are based on nucleic acid amplification tests such as line probe assay (LPA) test (GenoTypeMTBDR*plus*, Nehren, Germany)[3] and GeneXpert MTB/RIF assay (Cepheid Sunnyvale, CA).[4] LPA is technically a complicated assay and both the tests require costly equipment and reagents. Despite important advances in TB diagnostic, a simple, rapid, and accurate test with low cost and high operational efficacy remains elusive.[5] Upgrading the existing laboratories with

Access this article online

Quick Response Code:

Website: www.jgid.org

DOI: 10.4103/jgid.jgid_309_21

Address for correspondence: Dr. Raj Narayan Yadav, Department of Microbiology, National Institute of Tuberculosis and Respiratory Diseases, New Delhi, India.
E-mail: rajnarayan.aiims@gmail.com

How to cite this article: Yadav RN, Verma AK, Kaushik G. Laboratory cost analysis of conventional and newer molecular tests for diagnosis of presumptive multidrug-resistant tuberculosis patients. J Global Infect Dis 2022;14:93-8.

Received: 27 November 2021 **Revised:** 29 March 2022
Accepted: 29 April 2022 **Published:** 26 August 2022

newer rapid diagnostic techniques and creating new laboratory facilities are essential requirement to achieve the 2035 End TB strategy. There is a paucity of data to evaluate the laboratory cost of conventional and rapid diagnostic tests in high-TB burden countries such as India. In the present study, the cost of existing conventional methods for diagnosing presumptive MDR-TB patients was analyzed and compared to the cost of newer TB diagnostic techniques and with their various diagnostic scenarios, in a North Indian tertiary care center.

Methods

The study was conducted at the Mycobacteriology Laboratory, Department of Medicine, AIIMS, New Delhi, India. This is an autonomous institute of national importance. The laboratory is accredited as an intermediate laboratory by the Central TB Division, Ministry of Health and Family Welfare, Government of India.

A detailed costing of mycobacterial diagnostic tests with sputum samples was computed from laboratory perspective. Costs were collected for tests conducted routinely using AFB smear microscopy (Light Microscopy using Ziehl Neelsen [ZN] staining, and Light Emitting Diode-Fluorescent Microscopy (LED-FM) using Auramine "O" staining); sputum processing by NALC-NaOH method; mycobacterial culture, and DST of rifampicin and isoniazid using Lowenstein-Jensen solid media by 1% proportion method;[6] liquid culture system BACTEC MGIT 960 (BD Diagnostic systems, Sparks, MD, USA); LPA (Version 2.0); and GeneXpert MTB/RIF assay. Phenotypic DST was performed when culture test (using solid or liquid media) became *Mtb* positive. Costs were established using ingredient approach method (which involved estimating the total amounts of goods and services actually used in applying the test and multiplying them by their respective unit prices) as performed previously[7,8] for all procedural steps that were required for these tests starting from the receiving of samples until safe disposal of the waste materials.

Laboratory methods and testing performance

Sputum samples were subjected to all described methods including solid media and liquid system (BACTEC MGIT 960). Cultures were also identified for *Mtb* by biochemical (niacin and catalase) tests in case of solid DST and MPT64 antigen-based SD bioline immunochromatographic identification test in case of liquid DST. The MTBDR*plus* LPA was performed directly on the sputum samples or culture isolates as per the manufacturer's instructions. GT Blot (HainLifescience) instrument was used to carry out hybridization step of LPA. GeneXpert testing was conducted according to manufacturer's instructions directly from sputum samples using a 16-module instrument with automated readout. This test was performed with 32 samples processing per day. For the AFB smear, LPA, and mycobacterial culture, we have considered processing of 15 tests/day for 8 h. A total eight *Mtb* cultures isolates were considered for further processing using solid and liquid DST per working day. Laboratory testing load and frequency for detection *Mtb* and MDR-TB was computed based on laboratory records. Among presumptive MDR-TB patients referred for diagnosis, around 72.5% were AFB smear-positive and 27.5% were AFB smear-negative. The average culture positivity was found to be 64.3% and 71% by using solid and liquid media, respectively. Among smear-negative sputum samples, laboratory register showed the average yield of *Mtb* to be 9% and 14% by using solid and liquid media, respectively. LPA and GeneXpert MTB/RIF assay were mainly carried out directly from sputum samples and yielded *Mtb* in 66.2% (87% in AFB smear-positive and 10.4% AFB smear-negative) and 70.4% (91% in AFB smear-positive and 14% in AFB smear-negative) samples, respectively. The yield of MDR-TB by phenotypic DST and LPA methods were found to be 22% and 21%, respectively. GeneXpert MTB/RIF assay detected rifampicin-resistant *Mtb* in 23% samples.

Cost analysis

The staff time, consumable supplies, and equipment quantities utilized for each test were calculated through direct observation of testing procedures.[7] For the cost of equipment and consumable (kit) of MGIT, MPT64 antigen-based identification test, LPA, GeneXpert MTB/RIF assay, and LED-FM, we have applied the price, negotiated between Foundation for Innovative New Diagnostics (FIND) and the manufacturing companies, as India with many high TB burden countries-eligible for negotiated price.[9-12] Cost of equipment and consumable of NALC-NaOH processing, solid culture and DST, biochemical tests, and ZN-stained AFB microscopy were derived through quotations from various suppliers and from laboratory records during the year 2015. These cost estimates were computed in 2015 as United States dollars. Basic costs of key equipments and consumables are shown in Table 1. Cost of identification using MPT 64 antigen-based SD Bioline immunochromatographic identification test was merged with liquid DST (rifampicin and isoniazid) and, that of biochemical tests (catalase and niacin) were calculated with solid DST (rifampicin and isoniazid). Overhead laboratory cost (physical infrastructure and other operational cost) was calculated with quantity of physical infrastructure utilized by each test and annualized with 3% discount rate as described in other study.[7,8,13] Cost of the instruments was adjusted with annual and comprehensive maintenance cost. The lifetime of centrifuge, biosafety cabinet, and thermal cycler was estimated to be 10 years, while it was 5 years for other instruments. Costs that were shared among the techniques were allocated by identifying number of procedural steps involved in techniques. After that, the cost of each piece of equipment was split by the number of steps in which the equipment was utilized during the test procedure. The cost per step was then multiplied by the number of steps in which the equipment was utilized during the test to get the cost of particular test. Labor cost was calculated using salary structure issued by National TB Elimination Program (previously called the Revised National TB Control Program) and time spent for each test.

Table 1: Costs of key equipment and consumables

Instruments	Quantity	Actual cost in US dollars
Centrifuge	Per instrument	13666.4
Light microscope	Per instrument	3020
LED-fluorescent microscope	Per instrument	1640
BACTEC MGIT 960	Per instrument	38950
UPS Power supply	Per instrument	1845
Thermal cycler	Per instrument	7121.2
GT Blot	Per instrument	16029.3
GeneXpert XVI module	Per instrument	71500
Biosafety Cabinet	Per instrument	7444.7
Water bath	Per instrument	1298.7
Inspissator	Per instrument	6800.8
Consumables		
BBL MGIT tube	Per pack (100)	195
GenoTypeMTBDR*plus* kit	Per kit (96)	819.47
GeneXpert cartridge	Per cartridge	9.98
BACTEC MGIT IR kit	Per kit	36.3
SD BiolineTB Ag MPT64 kit	Per box (25)	45.2

Numbers in parentheses indicate number of tubes/test strips. Price listed here is without maintenance cost while it was included in main calculation. US: United States, LED: Light Emitting Diode, UPS: Uninterruptible Power Supply, MGIT: Mycobacterial Growth Indicator Tube, IR: Isoniazid and Rifampicin

We have also calculated the cost incurred for the detection of each *Mtb*[8] and MDR-TB. We have also analyzed the diagnostic cost associated with different hypothetical algorithm/scenarios. Incremental costs of diagnostic scenarios have been calculated from the cost associated with solid culture scenario. All invalid or contaminated samples were considered as test negative as done by previous workers.[7,8]

Results

Cost of each tuberculosis diagnostic test

The average cost per patient was cheaper for LED-FM ($2) as compared to conventional light microscopy using ZN staining method ($2.5). Basic costs for mycobacterial investigations found to be cheaper by using solid media as compared to liquid media. Cost per processed mycobacterial culture and DST by using solid media was calculated as $8 and $13.5, respectively; while the corresponding values by using liquid media (BACTEC MGIT 960) were found to be $12 and $17.1, respectively, as detailed in Table 2. Cost associated with each test by GeneXpert MTB/RIF assay was found to be less ($13.8) as compared to MTBDR*plus* LPA test ($18.6). The cost of LPA and GeneXpert MTB/RIF assay were largely attributable to consumables ($12.2 [65.6% of total cost] for LPA and $11.1 (80.4% of total cost) for GeneXpert MTB/RIF assay). Labor cost per test associated with GeneXpert MTB/RIF assay was lowest among all the tests described in the present study, whereas it was found to be high in phenotypic DST (by using solid and liquid media) and LPA. Both LPA and GeneXpert MTB/RIF assay are able to detect *Mtb*; and simultaneously LPA provided DST of rifampicin and isoniazid (and hence used for early detection of MDR-TB). On the other hand, GeneXpert MTB/RIF assay provided early detection of rifampicin-resistant TB (RR-TB) which is surrogate marker of MDR-TB.[14,15] LPA provided results in 2–3 days whereas, GeneXpert MTB/RIF assay provided results within a day (in 2 h).

The average diagnostic cost per patient was calculated with various proposed diagnostic algorithm as shown in Table 3. An average cost per patient for implementing solid culture scenario (LED- FM plus solid culture, and solid DST with culture-positive isolates) was found to be $18.7. This diagnostic scenario is time consuming and takes around 3 months to provide the results. Therefore, it was replaced by liquid culture scenario (LED-based microscopy plus liquid culture, and liquid DST with culture-positive samples) in many laboratories for rapid results. Cost per patient for diagnosis of TB using liquid culture scenario was calculated as $26.1 (incremental cost $7.4). However, this scenario also takes weeks to months for providing results. Therefore, rapid molecular methods with selective use of culture-based DST are being used in many laboratories for promptly initiation of accurate treatment. Such scenario using molecular LPA with liquid culture method (LED-FM, LPA with smear-positive samples, liquid culture with smear-negative samples, and again LPA with culture-positive isolates) would cost $19.5 (incremental cost $0.8). This cost is comparable to the cost using solid culture scenario and cheaper than those with liquid culture scenario. If GeneXpert MTB/RIF assay would be used alone at Point-of-Care, it would cost $13.8 per sample which is cheaper as compared to culture-based DST and LPA.

Cost for each identified multidrug-resistant tuberculosis patients

Costs per identified *Mtb* by culture tests were calculated as $12.4 and $16.9 using solid and liquid media, respectively. The yield of *Mtb* and MDR-TB varied substantially with the method applied; therefore, it contributed to different costs for the yield of each *Mtb* and MDR-TB. Cost per identified *Mtb* (with DST results) and MDR-TB by solid culture scenario were $29.1 and $132.2, respectively; and the corresponding values for liquid culture scenario were $36.9 and $167.5, respectively.

Discussion

In the recent years, major emphasis has been given to widespread availability of rapid diagnostic tests across the high TB-burden countries and prompt initiation of MDR-TB treatment. Therefore, upgradation of laboratory capacity with newer rapid tests for the detection of TB and MDR-TB is urgently required; however, it appears very costly. To overcome this challenge and to facilitate access to these diagnostic techniques, FIND has negotiated with the manufacturing partners to obtain significant price reduction (average 50% on equipment and 75% on consumables) in various tests for high TB-burden countries. In the present study, detailed cost of various TB diagnostic techniques was computed which would

Table 2: Component costs of each test for the diagnosis of presumptive multidrug-resistant tuberculosis patient

Diagnostic test	Consumable cost (in USD) (%)	Equipment cost (in USD) (%)	Labor cost (in USD) (%)	Overhead cost (in USD) (%)	Total cost (in USD)	Total cost (in INR)
ZN smear	0.2 (8)	0.2 (8)	1.2 (48)	0.9 (36)	2.5	156.8
LED-FM	0.2 (10)	0.1 (5)	0.8 (40)	0.9 (45)	2	128.9
L–J culture (Solid)	2.7 (33.8)	0.9 (11.2)	1.4 (18)	3 (37)	8	517.57
L–J DST (solid)	3.3 (24.4)	1.4 (10.4)	3.9 (28.9)	4.9 (36.3)	13.5	879
MGIT culture	8.7 (72.5)	1.3 (10.8)	0.9 (7.5)	1.13 (9.4)	12	778.6
MGIT DST	9.6 (56.1)	3.4 (19.9)	1.8 (10.5)	2.3 (13.5)	17.1	1109.6
GenoType MTBDR*plus*	12.2 (65.6)	2 (10.8)	2.2 (11.8)	2.2 (11.8)	18.6	1210
GeneXpert MTB/RIF assay	11.1 (80.4)	1.9 (13.8)	0.4 (2.9)	0.4 (2.9)	13.8	895.2

L-J DST and MGIT DST were carried out for RIF and INH. ZN: Ziehl Neelsen, L–J: Lowenstein-Jensen, RIF: Rifampicin, INH: Isoniazid, DST: Drug susceptibility testing, USD: United State Dollar, INR: Indian Rupees, TB: Tuberculosis, LED-FM: Light Emitting Diode-Fluorescent Microscopy, MGIT: Mycobacterial Growth Indicator Tube

Table 3: Laboratory cost analysis showing expected costs (in United States dollars) of different diagnostic scenarios for detection of *Mycobacterium tuberculosis* and multidrug-resistant tuberculosis strains

Scenarios	Average cost per sputum sample	Cost per detected Mtb with DST results	Cost per identified MDR-PTB/RR-TB
LED-FM plus solid culture and; plus solid DST on culture-positive isolates (solid culture scenario)	18.7 (Reference cost)	29.1 (Reference cost)	132.2 (Reference cost)
LED-FM plus liquid culture and; plus liquid DST on culture-positive isolates (liquid culture scenario)	26.1 (7.4)	36.9 (7.8)	167.5 (35.3)
LED-FM; plus LPA on smear-positive samples; plus GeneXpert MTB/RIF assay on smear-negative samples	19.3 (0.6)	28.9 (−0.2)	137.5 (5.3)
LED-FM plus LPA	20.7 (2)	31.2 (2.1)	148.8 (16.6)
LED-FM plus GeneXpert MTB/RIF assay	15.8 (−2.9)	22.4 (−6.7)	97.6 (−34.6)
LPA alone	18.7 (0.0)	28.2 (-0.9)	134.4 (2.2)
GeneXpert MTB/RIF assay alone	13.8 (−4.9)	19.7 (−9.4)	85.3 (−46.9)
GeneXpert MTB/RIF assay plus liquid culture; plus liquid DST on culture-positive isolates	38 (19.3)	53.5 (24.4)	232.7 (100.5)
GeneXpert MTB/RIF assay plus solid culture; plus solid DST on culture-positive isolates	30.5 (11.8)	44.5 (15.4)	202.3 (70.1)
LED-FM on all samples plus; LPA on smear-positive samples; plus liquid culture on smear-negative samples; with LPA on culture-positive isolates	19.5 (0.8)	29.2 (0.1)	139.2 (7)
LED-FM; LPA on smear-positive samples; plus solid culture on smear-negative samples; with LPA on culture-positive isolates	18.1 (−0.6)	27.8 (−1.3)	132.5 (0.3)
LED-FM; plus GeneXpert MTB/RIF assay on smear-positive samples; plus liquid culture on smear-negative samples; with GeneXpert MTB/RIF assay on culture-positive isolates	15.8 (−2.9)	22.7 (−6.4)	98.7 (−33.5)
LED-FM; plus GeneXpert MTB/RIF assay on smear-positive samples; plus solid culture on smear-negative samples; with GeneXpert MTB/RIF assay on culture-positive isolates	14.5 (−4.2)	21.3 (−7.8)	92.5 (−39.7)

RR-TB in place of MDR-TB was calculated with GeneXpert MTB/RIF assay. Incremental costs are shown in parentheses and have been calculated from the cost associated with solid culture scenario as a reference cost. LED-FM: LIGHT emitting diode-fluorescent microscopy, DST: Drug susceptibility testing, MDR-PTB: Multidrug resistant-pulmonary tuberculosis, Mtb: Mycobacterium tuberculosis, LPA: Line probe assay, RR-TB: Rifampicin-resistant tuberculosis, RIF: Rifampicin

help the laboratories in allocation of resources to facilitate various newer techniques or in upgrading the laboratory.

The LED-FM was found to be less costly ($2) as compared to ZN staining-based light microscopy ($2.5). Most of the cost savings were contributed by labor cost due to reduced amount of time required to read the slides and less equipment cost. The results of present study showed that the overall cost per test for diagnosis of MDR-PTB patient is comparable between L–J and LPA tests despite of actual cost of L–J media being cheaper than LPA kit. Furthermore, diagnostic costs of both molecular tests (LPA and GeneXpert MTB/RIF assay) was less as compared to cost with liquid culture-based DST (using MGIT 960) with additional advantage of early diagnosis. Therefore, we have designed various diagnostic scenarios in order to use these molecular tests.

As compared to solid culture scenario, the incremental cost per test for applying WHO endorsed rapid molecular tests in combination with selective use of liquid culture scenario

was found to be lower as compared to liquid culture scenario alone. The present study was carried out at the reference laboratory where most of the patients referred for diagnosis were *Mtb* culture positive. However, many laboratories may have less culture positivity rate. In such places, the diagnostic cost per patient by using liquid culture scenario alone would be reduced. Technical effectiveness of LPA has shown high sensitivity, specificity, and rapidity in AFB smear-positive patients,[16] but it has shown poor performance in smear-negative patients. Therefore, most of the laboratories perform LPA only on smear-positive sputum samples and phenotypic culture only on sputum samples with either smear-negative results or invalid LPA results to obtain higher yield at reduced turnaround time. Furthermore, the use of molecular method as an additional test with conventional culture-based DST was found to be costly as compared to the use of molecular method with selective use of culture-based DST.

To use rapid molecular tests as an alternative to culture-based DST, the Revised National TB Control Programme of India is now using a combination of LPA and GeneXpert MTB/RIF assay along with LED-FM at most reference laboratories. The diagnostic scenario may includes LED-FM, LPA with AFB smear-positive samples, and GeneXpert MTB/RIF assay on smear-negative samples. Cost per test and per identified MDR-TB/RR-TB with such scenario was found to be $19.3 and $137.5, respectively. These costs were found comparable with solid culture scenario and less as compared to liquid culture scenario. These findings indicate that the use of these molecular tests with selective use of culture-based DST is overall less costly as compared to using culture-based DST alone for early diagnosis of MDR-PTB patients. Early diagnosis of MDR-TB will be helpful for prompt initiation of accurate therapy and thus it will lead to reduction in the cost and side effects.[17] By detecting MDR-TB earlier, the samples can be subjected to further diagnosis for extensively drug-resistant TB (XDR-TB) sooner. This will be helpful in interruption of chain of transmission of drug-resistant TB in community and thus would be able to save more lives. Limitation of molecular method includes inability to differentiate dead and live bacilli and hence not very useful for following-up patients. India is heavily depending on liquid culture methods for detecting live *Mtb* bacilli during follow-up while patients are on treatment.

Although most of the instruments are available on FIND negotiated price, it requires substantial funding at the beginning to start these facilities. Managerial and administrative costs and the cost of transporting the samples were not included in the present study which may further raise the costs. The calculated costs cannot be considered as fixed because it can be changed with the proportion of samples processed per day and laboratory settings, rate of *Mtb* positivity etc., and would be applicable only for FIND negotiated cost applicable to high TB-burden countries. This study is mainly based on cost calculation from the laboratory perspective; and hence, cost-effective analysis with considering TB burden in population and accuracy parameters of diagnostic tests was not computed, which is limitation of the study.

Based on these findings, it is concluded that the use of LED-based microscopy is less costly as compared to light microscopy using ZN staining. The use of rapid molecular test with selective use of culture-based method is overall less costly as compared to the use of culture-based method alone at negotiated price. Early diagnosis can save more lives and interrupt TB transmission in the community. It is important to balance costs with tests performance parameter, burden of TB at point of care, and ability to provide early results before analyzing diagnostic scenario at place.

Research quality and ethics statement

The study was approved by the Institute Ethics Committee, All India Institute of Medical Sciences, New Delhi, India (RT-28/01.06.2012). The authors followed applicable EQUATOR Network (http://www.equator-network.org/) guidelines during the conduct of this research project.

Financial support and sponsorship

Nil

Conflicts of interest

There are no conflicts of interest.

References

1. World Health Organization. Global Tuberculosis Report; 2020. Available from: https://www.who.int/publications/i/item/9789240013131. [Last accessed on 2021 Sep 28].
2. Whitelaw A, Peter J, Sohn H, Viljoen D, Theron G, Badri M, *et al.* Comparative cost and performance of light-emitting diode microscopy in HIV-tuberculosis-co-infected patients. Eur Respir J 2011;38:1393-7.
3. WHO Policy Update. The use of Molecular Line Probe Assays for the detection of resistance to isoniazid and rifampicin. WHO/HTM/TB/2016.12. Available from: https://apps.who.int/iris/bitstream/handle/10665/250586/9789241511261-eng.pdf. [Last accessed on 2022 Mar 29].
4. WHO Policy Update. Xpert MTB/RIF Assay for the Diagnosis of Pulmonary and Extrapulmonary TB in Adults and Children. WHO Website; 2013. Available from: https://www.who.int/publications/i/item/9789241506335 [Last accessed on 2022 March 28].
5. Dowdy DW, O'Brien MA, Bishai D. Cost-effectiveness of novel diagnostic tools for the diagnosis of tuberculosis. Int J Tuberc Lung Dis 2008;12:1021-9.
6. Central TB Division, Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India, Revised National Tuberculosis Control Programme, Culture of *Mycobacterium tuberculosis* and Drug Susceptibility Testing on Solid Medium. Manual of Standard Operating Procedures. TBC India Website. Available from: https://tbcindia.gov.in/WriteReadData/l892s/7293794058standard%20operating%20procedures%20for%20C&DST%20labs.pdf f. [Last accessed on 2021 Sept 28].
7. Shah M, Chihota V, Coetzee G, Churchyard G, Dorman SE. Comparison of laboratory costs of rapid molecular tests and conventional diagnostics for detection of tuberculosis and drug-resistant tuberculosis in South Africa. BMC Infect Dis 2013;13:352.
8. Mueller DH, Mwenge L, Muyoyeta M, Muvwimi MW, Tembwe R, McNerney R, *et al*. Costs and cost-effectivness of tuberculosis cultures using solid and liquid media in a developing countries. Int J Tuberc Lung 2008;12:1196-202.
9. Prices for BACTEC and MGIT and Country List. Available from: https://www.finddx.org/pricing/bactec-mgit/[Last accessed on 2022 March 29].
10. Prices and Country List for Line Probe Assay and Associated

Instrumentation. Available from: https://www.finddx.org/pricing/genotype-mtbdr/. [Last accessed on 2022 Mar 29].
11. Price for Xpert® MTB/RIF and FIND Country List. Available from: https://www.finddx.org/pricing/. [Last accessed on 2022 Mar 29].
12. Prices for Primo Star iLED and Country List. Available from: https://www.finddx.org/pricing/primo-star-iled/. [Last accessed on 2022 Mar 29].
13. World Health Organization. WHO Guide to Cost-Effective Analysis; 2003. Available from: https://apps.who.int/iris/bitstream/handle/10665/42699/9241546018.pdf?sequence=1&isAllowed=y [Last accessed on 2022 Mar 29].
14. Sharma SK, Kohli M, Chaubey J, Yadav RN, Sharma R, Singh BK, *et al.* Evaluation of Xpert MTB/RIF assay performance in diagnosing extrapulmonary tuberculosis among adults in a tertiary care centre in India. Eur Respir J 2014;44:1090-3.
15. Sharma SK, Kohli M, Yadav RN, Chaubey J, Bhasin D, Sreenivas V, *et al.* Evaluating the diagnostic accuracy of Xpert MTB/RIF assay in pulmonary tuberculosis. PLoS One 2015;10:e0141011.
16. Yadav RN, Singh BK, Sharma SK, Sharma R, Soneja M, Sreenivas V, *et al.* Comparative evaluation of GenoType MTBDRplus line probe assay with solid culture method in early diagnosis of multidrug resistant tuberculosis (MDR-TB) at a tertiary care centre in India. PLoS One 2013;8:e72036.
17. Heymann SJ, Brewer TF, Ettling M. Effectiveness and cost of rapid and conventional laboratory methods for *Mycobacterium tuberculosis* screening. Public Health Rep 1997;112:513-23.