DOI: 10.7860/JCDR/2016/18837.7755

Original Article

Microbiology Section

Comparative Study of GeneXpert with ZN Stain and Culture in Samples of Suspected Pulmonary Tuberculosis

MONIKA AGRAWAL[1], ASHISH BAJAJ[2], VINAY BHATIA[3], SARJANA DUTT[4]

ABSTRACT

Introduction: Tuberculosis remains one of the deadliest communicable diseases. There are number of tests available for the diagnosis of tuberculosis but conventional microscopy has low sensitivity and culture although gold standard, takes longer time for positivity. On the other side, Nucleic acid amplification techniques due to its rapidity and sensitivity not only help in early diagnosis and management of tuberculosis especially in patients with high clinical suspicion like immunocompromised patients, history of contact with active tuberculosis patient etc., but also curtail the transmission of the disease.

Aim: To evaluate the sensitivity, specificity, positive predictive value and negative predictive value of Nucleic acid amplification assay (GeneXpert) using respiratory samples in patients with suspected pulmonary tuberculosis and compare with AFB smear microscopy (Ziehl Neelsen stain) and Acid Fast Bacilli (AFB) culture.

Materials and Methods: We retrospectively reviewed the respiratory samples of suspected pulmonary tuberculosis (including Bronchoalveolar lavage and sputum) of 170 patients from Jan 2015 to Nov 2015 for ZN stain, culture and GeneXpert (Xpert® MTB/Rif assay). The sensitivity, specificity, PPV and NPV of GeneXpert and ZN microscopy were calculated using Liquid culture of *Mycobacterium tuberculosis* as gold standard.

Results: A total of 170 patient samples were evaluated in final analysis. Of these, 14 samples were positive by all three methods used in our study. The overall sensitivity, specificity, PPV and NPV of GeneXpert were 86.8%, 93.1%, 78.5% and 96% respectively and for BAL sample, 81.4%, 93.4%, 73.3% and 95.7% respectively. The overall sensitivity and specificity of AFB smear microscopy were 22.2%, and 78.5% respectively and for BAL sample 22.2% and 100% respectively. For AFB negative samples sensitivity and specificity were 79.1% and 93.1% respectively.

Conclusion: GeneXpert has a higher sensitivity than AFB smear microscopy in respiratory samples. GeneXpert can be a useful tool for early diagnosis of patients with high clinical suspicion of pulmonary tuberculosis. Positive GeneXpert, but culture negative results should be read cautiously and be well correlated with clinical and treatment history of the patient. The other major advantage of Gene Xpert is that it simultaneously detects Rifampicin resistance and is especially beneficial in patient with MDR and HIV associated tuberculosis and should be studied further.

Keywords: Acid fast bacilli, Bronchoalveolar lavage, Smear microscopy, Sputum

INTRODUCTION

According to the Global Tuberculosis report 2014 of World Health Organization (WHO), Tuberculosis (TB) remains one of the world's deadliest communicable diseases that is caused by the Bacterium *Mycobacterium tuberculosis* (MTB) [1]. The disease usually affects the lungs (pulmonary TB) and spread by air transmission from people with pulmonary TB [2]. In 2013, out of the estimated global annual incidence of 9 million TB cases, India alone shares the incidence of 2.1 million (24%) cases/year (one fourth of global incidence) [3].

Early diagnosis is imperative for early patient management and successful patient outcomes. False-negative results and misdiagnosis of TB suspects are common in developing nations, as most TB control programmes use Ziehl-Neelsen (ZN) smear microscopy, which has poor sensitivity and multiple visits are required that leads to higher default. Mycobacterial culture, although considered as the gold standard but is slow and usually takes 2-6 weeks time to yield a final result and requires proper infrastructure and technical expertise [1,4,5].

There are number of Nucleic Acid Amplification (NAA) methods that have been developed for rapid detection and identification of *Mycobacterium tuberculosis* (MTB) in clinical specimens of pulmonary and extra-pulmonary tuberculosis cases [6-8]. These techniques not only provide the advantage of rapidity of diagnosis but also detect even low MTB genomic copies in various specimens.

More recently, the WHO endorsed the GeneXpert (Xpert® MTB/Rif assay) for the diagnosis of TB [6]. The GeneXpert utilizes a DNA-PCR technique for simultaneous detection of *Mycobacterium tuberculosis* and Rifampicin resistance related mutations. It is the first fully automated bench top cartridge based nucleic acid amplification (CB-NAAT) assay for TB detection that includes all necessary steps of DNA PCR. It gives results within 2 hours. Diagnostic accuracy of GeneXpert for pulmonary TB has been reported high [9,10]. Patients with high risk of tuberculosis like presumptive HIV-associated TB patients and pediatric presumptive including extra pulmonary cases in whom AFB smear examination is usually negative, are the most likely to be benefited from GeneXpert [3,10].

AIM

The aim of this study was to evaluate the sensitivity, specificity, PPV and NPV of GeneXpert assay in patients with smear positive and smear negative respiratory samples (Preferably BAL samples) of suspected pulmonary tuberculosis and compared with AFB smear microscopy (ZN stain) and Liquid AFB culture.

MATERIALS AND METHODS

Inclusion criteria

Patients with clinical suspicion of pulmonary tuberculosis including symptoms of cough with or without expectoration for >2 weeks, weight loss, fatigue, haemoptysis and loss of appetite.

Exclusion Criteria

1) Samples received without clinical history
2) Samples received without request of all three tests
3) Patient with history of lung malignancies or fungal infections

Pulmonary specimens of 170 patients with suspected pulmonary tuberculosis, received retrospectively for the request of ZN microscopy, liquid AFB culture and GeneXpert from different centers to Oncquest lab ltd., were reviewed from a period of January 2015 to November 2015. Pulmonary specimens included 21 sputum and 149 BAL samples. Patient related information was collected from the Test Requisition Forms (TRF), received with the sample.

Laboratory Methods

Each sputum and BAL samples received in the lab from the centers as per the collection and transportation policy of the laboratory, were divided into three parts; one part was immediately tested using GeneXpert, second part used for ZN smear microscopy and third part for MGIT BACTEC 320 liquid culture and performed on same day. Only one sample either BAL or sputum from a single patient was divided and processed. For Liquid culture as much as sample was taken after sending for GeneXpert and ZN stain but it should be checked that volume remaining should not be less than 2 ml for processing.

GeneXpert testing was performed according to the manufacturer's instructions [11]. Sample reagent was added to untreated sputum and BAL at a ratio of 2:1, manually agitated and kept for 10 min at room temperature, then shaken again and kept for 5 min; 2 ml of the inactivated material was transferred to the test cartridge and inserted into the test platform. Only electronic results were used for comparison. Direct Smear microscopy was performed to investigate presence of acid fast bacilli with the second part of the specimen using conventional ZN staining method. Slides showing red coloured acid fast bacilli were taken as positive and negative slides were those without any acid fast bacilli [12].

Third part was processed using the N-acetyl-L cysteine- sodium hydroxide method (NALC-NaOH) as per the manufacturer's instructions, cultured on MGIT media and incubated in MGIT BACTEC 320 liquid culture system [13]. Sodium hydroxide (NaOH) is a decontaminating agent and also acts as emulsifier and NALC acts as a mucolytic agent and also reduces the concentration of NaOH required [12]. When the tubes were flagged positive by the system, ZN staining and culture on 5% sheep blood agar were performed from the tube directly to see any contamination as per the manufacturer's instructions. All tubes were checked for positivity till 42 days. MOTT and *Mycobacterium tuberculosis* testing from positive culture tubes were done by rapid immunochromatography test kit using MPT 64 antigen according to the manufacturer's instructions.

Analysis

The data was tabulated in Microsoft excel spreadsheet in a master chart and studied for correlation. Stastical analysis of the data was conducted with stastical package for the social science system version SPSS17.0. Sensitivity, specificity, PPV and NPV was calculated.

The sensitivity, specificity, PPV and NPV for the diagnosis of Pulmonary tuberculosis was calculated for AFB smear microscopy and the GeneXpert, using culture of *Mycobacterium tuberculosis* from sputum or BAL specimens as gold standard.

By taking culture method as reference, samples that were positive and negative in culture were considered true positive and true negative. Culture negative and GeneXpert positive samples were taken as false positive samples. GeneXpert negative and culture positive samples were considered false negative.

RESULTS

A total of 170 respiratory specimens (149 BAL and 21 Sputum samples) were tested. Of the 170 specimens, 14 samples were positive and 123 specimens were negative by all three methods used. Among 170 samples, 42 samples (24.7%) were GeneXpert TB positive. Among the 149 BAL samples, 22 samples were culture and GeneXpert positive, 8 samples were GeneXpert positive and 5 samples were only culture positive.

Among the 21 Sputum samples, 11 samples were culture and GeneXpert positive, 1 sample was GeneXpert positive [Table/Fig-1].

Altogether, 38 (22%) specimens were culture positive for AFB; 35 (20%) isolates were found to belong to MTB (11 were from sputum specimens, 24 were from BAL specimen), while the remaining 3 (1.7%) strains from BAL samples were identified as Mycobacterium other than tuberculosis (MOTT) species. Further speciation of these isolates was not done. Out of 170 samples, only 14 samples (6 BAL and 8 sputum samples) were found AFB smear positive. All these AFB smear positive samples were culture and GeneXpert positive [Table/Fig-2].

Among 156 AFB smear microscopy negative samples, 123 samples were negative for all three methods. In rest 33 AFB smear negative samples, 19 samples were culture and GeneXpert positive, 9 samples were GeneXpert positive and culture negative and 5 samples were culture positive and GeneXpert negative.

Overall sensitivity, specificity, PPV and NPV of GeneXpert when culture was taken as reference method is illustrated in [Table/Fig-3].

Overall sensitivity, specificity, PPV and NPV of AFB smear microscopy and in BAL when culture was taken as reference method is shown in [Table/Fig-4].

	Culture			
	BAL		Sputum	
Xpert TB	Positive	Negative	Positive	Negative
Positive	22	8	11	1
Negative	5	114	0	9

[Table/Fig-1]: Comparison of results from GeneXpert with culture as gold standard.

	Culture			
	BAL		Sputum	
AFB stain	Positive	Negative	Positive	Negative
Positive	6	0	8	0
Negative	21	122	3	10

[Table/Fig-2]: Comparison of results from AFB smear and culture on as gold standard.

Specimen type	Sensitivity	Specificity	PPV	NPV
All samples (n=170)	86.8%	93.1%	78.5%	96%
AFB negative (n=156)	79.1%	93.1%	67.8%	96%

[Table/Fig-3]: Sensitivity, specificity, PPV and NPV values of GeneXpert overall with culture as gold standard.

Specimen type	Sensitivity	Specificity	PPV	NPV
BAL	22.2%	100%	100%	85.3%
Sputum	72.7%	100%	100%	76.9%

[Table/Fig-4]: Sensitivity, specificity, PPV and NPV values of ZN stain with culture as gold standard

Specimen type	Sensitivity	Specificity	PPV	NPV
BAL	81.4%	93.4%	73.3%	95.7%
Sputum	100%	90%	91.6%	100%

[Table/Fig-5]: Sensitivity, specificity, PPV and NPV values of the GeneXpert with culture as gold standard.

Sensitivity, specificity, PPV and NPV of GeneXpert in BAL and for sputum samples is depicted in [Table/Fig-5].

For AFB negative samples sensitivity, specificity, PPV and NPV was 79.1%, 93.1%, 67.8% and 96% respectively. For AFB smear positive samples, sensitivity and PPV were 100% [Table/Fig-3].

DISCUSSION

In this retrospective study, we have evaluated the diagnostic yield of Gene Xpert to detect MTB in respiratory samples (BAL and Sputum) and compared it with AFB culture which was taken as gold standard.

Mycobacterial cultures for detection of *Mycobacterium tuberculosis* can be done either using solid (Lowenstein Jensen media) or liquid broth system (MGIT 320). Results by MGIT liquid culture medium come earlier as compared to LJ medium [14,15] In our study, results from MGIT 320 culture were included. GeneXpert is a simple bench top point of care diagnostic assay that can be performed with minimal training. The results are available within 2 hours, much earlier than the culture which usually takes days to come positive [10,16].

Numbers of studies have demonstrated the utility of GeneXpert in diagnosis of pulmonary tuberculosis [17-20]. In our study, overall sensitivity, specificity, PPV and NPV of GeneXpert were 86.8%, 93.1%, 78.5% and 96% respectively that is comparable with other studies [21-24]. In the other studies, GeneXpert sensitivity and specificity for BAL sample was from 81%-92% and 71%-100%, it is in conjunction with our study as shown in [Table/Fig-6] [21,22,24-26]. Although specificity in our study is 93.4%, it is because 3 culture samples were positive for MOTT and GeneXpert only detects MTB. In other two samples, although MTB growth is in culture but it is possible that the bacterial load may have been too low for the GeneXpert to detect the DNA from MTB- complex. It shows that a patient with a negative GeneXpert can still have TB with MTB or MOTT [21,25,27]. The NPV value of GeneXpert is high in our study in comparison to the study done by Kanwal et al., as LJ media was used in their study whereas in our and other studies, liquid culture method was used [26] [Table/Fig-6,7].

Study	Study Design	Sen	Spec	PPV	NPV
Pierrae et al., [21]	Retrospective	80	98.6	88.9	97.2
HY Lee et al., [22]	Retrospective	81.6	100	100	92.1
Dewald et al., [25]	Retrospective	92.3	87.7	80.0	95.5
Kanwal et al., [26]	Prospective	91.86	71.42	97.53	41.66
Surendra et al., [24]	Prospective	90	100	100	98.1
Our study	Retrospective	81.4%	93.4%	73.3%	95.7%

[Table/Fig-6]: Comparison of Sensitivity, Specificity, PPV and NPV of GeneXpert in BAL samples in different studies [21,22,24-26].

Study	Sen	Spec	PPV	NPV
Pierrae et al., [21]	25	95.8	45.5	90.1
Dewald et al., [25]	41.0	98.6	94.1	75.8
Kanwal et al., [26]	39.53	100	100	11.86
Our study	22.2%	100%	100%	85.3%

[Table/Fig-7]: Comparison of Sensitivity, Specificity, PPV and NPV of smear microscopy in BAL samples in different studies [21,25,26].

9 samples which were culture negative and GeneXpert positive (specificity- 93.1% overall), the result of GeneXpert was very low or low positive. As cases were evaluated retrospectively, history of treatment with ATT cannot be ruled out with low bacterial load. PCR test amplifies any DNA, of live or dead bacilli. Therefore while diagnosing a person with active tuberculosis clinicians need to be very cautious using it as a sole method. Clear history of treatment with ATT is required to avoid false positive results [16,25].

In comparison with culture used as gold standard, sensitivity, specificity, PPV and NPV for Smear microscopy for BAL sample were recorded as 22.2%, 100%, 100% and 85.3% respectively, which is in line with other studies as depicted in [Table/Fig-7] [21,25,26].

GeneXpert assay had an overall sensitivity of 86.8% and for BAL sample 81.4% for PTB, which is superior to that of smear microscopy (overall 36.8% and for BAL 22.2%). Overall Specificities of GeneXpert and smear microscopy were 93.1% and 100% respectively which also correlate well with other studies [21,25,26].

For smear negative samples Sensitivity n specificity of GeneXpert is 79.1% and 93.1% that correlate well with other studies from 57%-75% and 97%-100% respectively [27-30] For smear positive cases sensitivity is 100% in line with other studies from 68.6%-100% [27-30].

Sensitivity and specificity of GeneXpert in sputum assay in our study is 100% and 90% that is line with the study of Sharma et al., (96.9% and 99.8%) [24].

Our study further strengthens the use of GeneXpert in smear positive pulmonary samples as endorsed by WHO [10]. In patients with incongruous results of smear microscopy and GeneXpert pulmonary samples but high clinical evidence of pulmonary tuberculosis like HIV positive or critically ill, clinicians may exercise their clinical decision to start anti tubercular treatment after sending sample for culture [6].

However, GeneXpert does not eliminate the need of conventional microscopy, culture and anti-tubercular drug sensitivity that are required to monitor the progression of treatment and to detect resistance to drugs other than Rifampicin [6].

LIMITATIONS

There were certain limitations of the study: First, the study was performed retrospectively and results couldn't be correlated with radiological findings and histo-pathological reports. Second, one of the important strength of the Xpert assay is its ability to detect the presence of Rifampicin resistance. The sensitivity and specificity of MTB/RIF assay to detect Rifampicin resistance in our study was not evaluated and not included in our objective as we didn't get the requisition for Rifampicin sensitivity by phenotypic method in all the positive samples. Third, as number of sputum samples present in this study is less, further studies with more number of samples need to be done.

CONCLUSION

GeneXpert and AFB smear microscopy share almost same specificity but sensitivity of GeneXpert is much higher than AFB smear microscopy in respiratory samples. Although culture is considered as a gold standard method but as it takes days to come positive and simultaneous detection of Rifampicin resistance is not possible with it. On other side GeneXpert can be a useful diagnostic method in patients of suspected pulmonary tuberculosis either AFB smear negative or positive due to its rapidity and simultaneous detection of Rifampicin resistance especially beneficial in patient with MDR and HIV associated tuberculosis. Cost effectiveness of GeneXpert in low income countries like India with high prevalence of tuberculosis need to be done.

Positive GeneXpert, but culture negative results need to be read cautiously and should be well correlated with clinical and treatment history of the patient.

ACKNOWLEDGMENTS

The authors are thankful to the management of Oncquest laboratories limited for supporting the work.

REFERENCES

[1] World Health Organization. Global tuberculosis report 2014. Geneva: WHO; 2014. Available from: http://apps.who.int/iris/bitstream/10665/137094/1/9789241564809_eng.pdf?ua=1

[2] Tuberculosis [Internet]. World Health Organization [cited 2015 may 1]. Available from: http://www.who.int/mediacentre/factsheets/fs104/en/.

[3] Annual status report, TB India 2015 http://webcache.googleusercontent.com/search?q=cache:ifkstKlE98oJ:www.tbcindia.nic.in/index1.php%3Flang%3D1%26level%3D1%26sublinkid%3D4160%26lid%3D2807+&cd=1&hl=en&ct=clnk&gl=in

[4] Evans CA. GenXpert – a game changer for tuberculosis control? *PLOS MED*. 2011;8:e1001064.

[5] Centers for Disease Control and Prevention (CDC). Updated guidelines for the use of nucleic acid amplification tests in the diagnosis of tuberculosis. MMWR *Morb Mortal Wkly Rep*. 2009;58:7-10.

[6] International standard for tuberculosis care, 3rd edition, 2014 www.who.int/tb/publications/standards-tb-care-2014/

[7] Piersimoni C, Scarparo C, Piccoli P, et al. Performance assessment of two commercial amplification assays for direct detection of *Mycobacterium tuberculosis* complex from respiratory and extrapulmonary specimens. *J Clin Microbiol*. 2002;40:4138-42.

[8] Saglam L, Akgun M, Aktas E. Usefulness of induced sputum and fibreoptic bronchoscopy specimens in the diagnosis of pulmonary tuberculosis. *J Int Med Res.* 2005;33:260-65.

[9] Shah I, Gupta Y. Role of molecular tests for diagnosis of tuberculosis in children. *Pediatric Oncall Journal*. 2015;12(1): www.pediatriconcall.com/Journal/Article/

[10] World Health Organization: Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert mtb/rif system. Policy statement 2011. http://whqlibdoc.who.int/publications/2011/9789241501545_eng.pdf.

[11] Xpert MTB RIF kit insert http://www.cepheid.com/manageddownloads/xpert-mtb-rif-english-package-insert-301-1404-rev-b-february-2015.pdf

[12] Forbes BA, Sahm DF, Weissfeld AS. Bailey and Scott's Diagnostic Microbiology, 12th edition. The C.V Mosby Co. St.Louis. 2007, chapter 45 Pg: 478-509.

[13] MGIT ™ Procedurel Manual http://www.finddiagnostics.org/export/sites/default/resource-centre/find_reports/pdfs/mgit_manual_nov2006.

[14] Sun JR, Lee SY, Perng CL, Lu JJ. Detecting *Mycobacterium tuberculosis* in Bactec MGIT 960 cultures by in house IS6110- based PCR assay in routine clinical practice. *J Formos Med Assoc*. 2009;108:119-25.

[15] Zhao P, Fang F, Yu Q, Guo J, Zhang JH, Qu J, et al. Evaluation of Bactec MGIT 960 system for testing susceptibility of *Mycobacterium tuberculosis* to first-line drugs in China. *PLoSOne*. 2014;9:e99659.

[16] Van Rie A, Page-Shipp L, Scott L, Sanne I, Stevens W. Xpert(®) MTB/RIF for point-of-care diagnosis of TB in high-HIV burden, resource-limited countries: hype or hope? *Expert Rev Mol Diagn*. 2010;10(7):937–46.

[17] Bowles EC, Freyée B, van Ingen J, Mulder B, Boeree MJ, van Soolingen D. Xpert MTB/RIF®, a novel automated polymerase chain reaction–based tool for the diagnosis of tuberculosis. *Int J Tuberc Lung Dis*. 2011;15:988–89.

[18] Malbruny B, Le Marrec G, Courageux K, Leclercq R, Cattoir V. Rapid and efficient detection of *Mycobacterium tuberculosis* in respiratory and non-respiratory samples. *Int J Tuberc Lung Dis*. 2011;15:553–55.

[19] Marlowe EM, Novak-Weekley SM, Cumpio J, Sharp SE, Momeny MA, Babst A, et al. Evaluation of the Cepheid Xpert MTB/RIF assay for direct detection of *Mycobacterium tuberculosis* complex in respiratory specimens. *J Clin Microbiol.* 2011;49:1621–23.

[20] Miller MB, Popowitch EB, Backlund MG, Ager EP. Performance of Xpert MTB/RIF RUO assay and IS*6110* real-time PCR for *Mycobacterium tuberculosis* detection in clinical samples. *J Clin Microbiol*. 2011;49:3458–62.

[21] Pierre Le Palud P, Cattoir V, Malbruny B, Magnier R, Campbell K, Oulkhouir Y, et al. Retrospective observational study of diagnostic accuracy of the Xpert® MTB/RIF assay on fiberoptic bronchoscopy sampling for early diagnosis of smear-negative or sputum-scarce patients with suspected tuberculosis. *BMC Pulm Med.* 2014;14 (1):137.

[22] Lee HY, Seong MW, Park SS, Hwang SS, Lee J, Park YS, et al. Diagnostic accuracy of Xpert® MTB/RIF on bronchoscopy specimens in patients with suspected pulmonary tuberculosis. *Int J Tuberc Lung Dis*. 2013;17(7):917–21.

[23] Chang K, Lu W, Wang J, Zhang K, Jia S, Li F, et al. Rapid and effective diagnosis of tuberculosis and rifampicin resistance with Xpert MTB/RIF assay: a meta-analysis. *J Infect.* 2012;64(6):580–88.

[24] 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. www.journals.plos.org/plosone/article?id=10.1371/journal.pone.0141011

[25] Barnard DA, Irusen EM, Bruwer JW, Plekker D, Whitelaw AC, Deetlefs JD, et al. Koegelenberg The utility of Xpert MTB/RIF performed on bronchial washings obtained in patients with suspected pulmonary tuberculosis in a high prevalence setting. *BMC Pulm Med*. 2015;15:103.

[26] Khalil KF, Butt T. Diagnostic yield of bronchoalveolar lavage gene xpert in smear-negative and sputum-scarce pulmonary tuberculosis. *Journal of the College of Physicians and Surgeons Pakistan*. 2015;25(2):115-18.

[27] Norin J (May, 2015) A retrospective evaluation study of diagnostic accuracy of Xpert® MTB/RIF assay, used for detection of *Mycobacterium tuberculosis* in Greece. http://www.diva-portal.se/smash/get/diva2:825390/FULLTEXT01.pdf

[28] Zeka AN, Tasbakan S, Cavusoglu C. Evaluation of the genexpert mtb/rif assay for rapid diagnosis of tuberculosis and detection of rifampin resistance in pulmonary and extrapulmonary specimens. *J Clin Microbiol.* 2011;49:4138-41.

[29] Armand S, Vanhuls P, Delcroix G, Courcol R, Lemaître N. Comparison of the Xpert MTB/RIF test with an IS6110-TaqMan real-time PCR assay for direct detection of Mycobacterium tuberculosis in respiratory and nonrespiratory specimens. *J Clin Microbiol*. 2011;49:1772–76.

[30] Zmak L, Jankovic M, Katalinic Jankovic V. Evaluation of Xpert MTB/RIF assay for rapid molecular diagnosis of tuberculosis in a two-year period in Croatia www.sciencedirect.com/science/article/pii/S2212553113000538.

PARTICULARS OF CONTRIBUTORS:

1. Consultant Microbiologist, Department of Microbiology, Oncquest Laboratories Limited, New Delhi, India.
2. Junior Consultant Microbiologist, Department of Microbiology, Oncquest Laboratories Limited, New Delhi, India.
3. Manager Molecular Biology, Department of Molecular Biology, Oncquest Laboratories Limited, New Delhi, India.
4. Director, Department of Molecular Biology and R&D, Oncquest Laboratories Limited, New Delhi, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Monika Agrawal,
H.No. 364, Sector 31, Gurgaon-122001, India.
E-mail: vanshvivaan@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Jan 13, 2016**
Date of Peer Review: **Feb 06, 2016**
Date of Acceptance: **Mar 25, 2016**
Date of Publishing: **May 01, 2016**