

Original Article

Evaluation of the accuracy of Xpert MTB/RIF assay in comparison to Liquid culture in extrapulmonary tuberculosis (EPTB) patients

¹Piyush Srivastava, ²Anshumali Srivastava¹Assistant Professor, TS Misra Medical College, Lucknow, Uttar Pradesh, India;²Professor, Career Institute of Medical Sciences and Hospital, Lucknow, Uttar Pradesh, India**ABSTRACT:**

Background: Evidence from 138 studies published before 2008 suggested that nucleic acid amplification technologies (NAAT) could not replace conventional mycobacterial tests (microscopy, culture) for diagnosing pulmonary and, especially, extrapulmonary tuberculosis (EPTB). The present study was conducted for assessing the accuracy of Xpert MTB/RIF assay in comparison to Liquid culture in extrapulmonary tuberculosis (EPTB) patients. **Materials & methods:** The present study was conducted for assessing the accuracy of Xpert MTB/RIF assay in comparison to Liquid culture in extrapulmonary tuberculosis (EPTB) patients. A total of 50 patients with extrapulmonary tuberculosis were assessed. Complete demographic and clinical details of all the patients were obtained. Extra-pulmonary specimens were collected in a sterile container and were assessed. Specimen thus collected was subjected to liquid culture and Xpert MTB/RIF. Results were analysed by SPSS software. **Results:** Overall, the sensitivity and specificity of Xpert MTB/RIF assay was 45.6% and 61.9% respectively. The sensitivity and specificity of Xpert MTB/RIF assay for Ascitic fluid specimen was 100% and 65.5% respectively. The sensitivity and specificity of Xpert MTB/RIF assay for Lymph node biopsy was 76% and 66.2% respectively. The sensitivity and specificity of Xpert MTB/RIF assay for pleural fluid specimen was 25.2% and 41.9% respectively. **Conclusion:** The GeneXpert MTB/RIF test has significant sensitivity and specificity for the diagnosis of EPTB.

Key words: Xpert MTB/RIF assay, Extrapulmonary tuberculosis

Received: 12 September 2018

Accepted: 19 October 2018

Corresponding Author: Anshumali Srivastava, Professor, Career Institute of Medical Sciences and Hospital, Lucknow, Uttar Pradesh, India**This article may be cited as:** Srivastava P, Srivastava A. Evaluation of the accuracy of Xpert MTB/RIF assay in comparison to Liquid culture in extrapulmonary tuberculosis (EPTB) patients. J Adv Med Dent Scie Res 2018;6(11):157-159.**INTRODUCTION**

Evidence from 138 studies published before 2008 suggested that nucleic acid amplification technologies (NAAT) could not replace conventional mycobacterial tests (microscopy, culture) for diagnosing pulmonary and, especially, extrapulmonary tuberculosis (EPTB). Only a few years later, GeneXpert technology has changed this paradigm, with a recent systematic review showing pooled sensitivity of 88% and pooled specificity of 98% for diagnosis of pulmonary TB, but evidence (as of March 2012) for using Xpert MTB/RIF for diagnosing EPTB is still comparatively weak.¹⁻⁴ Globally, there is still a dearth of studies involving the use of Xpert MTB/RIF in EPTB specimens, and few provide definitive answers. This is due mostly to the studies having small sample sizes across a range of various specimen types and differences in preprocessing methodologies and in input volumes

and to studies having been conducted in different populations (adults, children, HIV infected). In one large published study, the overall sensitivity of Xpert MTB/RIF on tissue biopsy specimens/fine-needle aspirates (FNA), pleural fluid, gastric aspirates, pus, cerebrospinal fluid (CSF), urine, and peritoneal/synovial/pericardial fluid was reported as 81% (95% confidence interval [95% CI], 76% to 86%), with specificity of 99.8% (95% CI, 99% to 100%).³⁻⁵

In contrast to pulmonary TB, the diagnosis of EPTB is still a serious problem in industrialised countries, where it remains undetected for a long time in a considerable number of cases. A major hindrance to the diagnosis of EPTB is the atypical presentation, often simulating neoplasia and/or inflammatory disorders. Furthermore in the non-respiratory specimens the bacterial load is generally very low, therefore strongly affecting the sensitivity of rapid

tests such as acid-fast microscopy and nucleic acid amplification (NAT).⁶⁻⁸ Hence; the present study was conducted for assessing the accuracy of Xpert MTB/RIF assay in comparison to Liquid culture in extrapulmonary tuberculosis (EPTB) patients

MATERIALS & METHOD

The present study was conducted for assessing the accuracy of Xpert MTB/RIF assay in comparison to Liquid culture in extrapulmonary tuberculosis (EPTB) patients. A total of 50 patients with extrapulmonary tuberculosis were assessed.

INCLUSION CRITERIA

- 1) Patients of both sexes and all age groups.
- 2) Patients who gave informed consent

Complete demographic and clinical details of all the patients were obtained. Extra-pulmonary specimens were collected in a sterile container and were

assessed. Specimen thus collected was subjected to liquid culture and Xpert MTB/RIF. Results were analysed by SPSS software.

RESULTS

Mean age of the patients was 42.5 years. Out of 50 patients, 32 samples were of pleural fluid, while 10 samples were Ascitic fluid. Remaining 8 samples were of lymph node biopsy. Overall, the sensitivity and specificity of Xpert MTB/RIF assay was 45.6% and 61.9% respectively. The sensitivity and specificity of Xpert MTB/RIF assay for Ascitic fluid specimen was 100% and 65.5% respectively. The sensitivity and specificity of Xpert MTB/RIF assay for Lymph node biopsy was 76% and 66.2% respectively. The sensitivity and specificity of Xpert MTB/RIF assay for pleural fluid specimen was 25.2% and 41.9% respectively.

Graph 1: Distribution of extrapulmonary samples

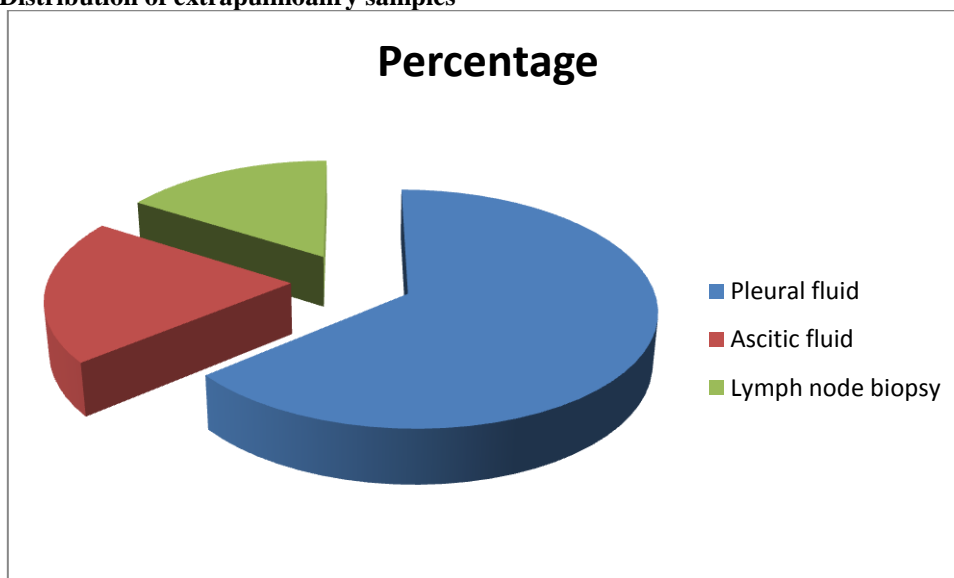


Table 1: Sensitivity and specificity of Xpert MTB/RIF assay

Specimens	Sensitivity	Specificity
Ascitic fluid	100%	65.5%
Lymph node biopsy	76%	66.2%
Pleural fluid	25.2%	41.9%
Overall	45.6%	61.9%

DISCUSSION

Nucleic acid amplification tests for rapid TB diagnosis are increasingly being used. The US CDC recommends that nucleic acid amplification tests be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB. However, no recommendation exists for their use in the investigation of patients suspected of having EPTB as the evidence base is limited. The Xpert® MTB/RIF assay (Cepheid Inc., CA, USA) marks an important development in the field of rapid molecular TB diagnostics. This multifunctional diagnostic

platform is an automated, closed system that performs real-time PCR and can be used by operators with minimal technical expertise, enabling diagnosis of TB and simultaneous assessment of rifampicin resistance to be completed within 2 h.⁶⁻⁸

Mean age of the patients was 42.5 years. Out of 50 patients, 32 samples were of pleural fluid, while 10 samples were Ascitic fluid. Remaining 8 samples were of lymph node biopsy. Overall, the sensitivity and specificity of Xpert MTB/RIF assay was 45.6% and 61.9% respectively. The sensitivity and specificity of Xpert MTB/RIF assay for Ascitic fluid

specimen was 100% and 65.5% respectively. Only a single published study from South Africa has previously assessed the use of Xpert for diagnosis of TB in children, but only respiratory samples were tested. For sputum culture-positive disease, Xpert MTB/RIF performed on two induced sputum samples detected 75.9% of TB cases compared with 37.9% using smear microscopy. This compares to a sensitivity of 86.9% (95% CI: 80–93) using Xpert MTB/RIF for EPTB in children in the study by Tortoli and colleagues. Unfortunately, failure to report the absolute number of children included, the number of samples tested per child and the actual numbers of each sample type from children precludes full appreciation of the data. Nevertheless, these data, together with those from Nicol and colleagues, provide some important progress in the arena of pediatric TB diagnosis, which remains a huge challenge.⁸⁻¹⁰

The sensitivity and specificity of Xpert MTB/RIF assay for Lymph node biopsy was 76% and 66.2% respectively. The sensitivity and specificity of Xpert MTB/RIF assay for pleural fluid specimen was 25.2% and 41.9% respectively. Chakravorty S et al developed the Xpert MTB/RIF Ultra assay (Ultra) to improve performance. Ultra and Xpert limits of detection (LOD), dynamic ranges, and RIF-R *rpoB* mutation detection were tested on *Mycobacterium tuberculosis* DNA or sputum samples spiked with known numbers of *M. tuberculosis* H37Rv or *Mycobacterium bovis* BCG CFU. Both tests had a specificity of 98.7% (95% CI, 93.0, 100), and both had comparable accuracies for detection of RIF-R in these samples. Ultra should significantly improve TB detection, especially in patients with paucibacillary disease, and may provide more-reliable RIF-R detection.¹¹ Rice JP et al evaluated the performance of Xpert MTB/RIF using clinical sputum specimens routinely collected from suspect pulmonary TB patients over a 4-year time period in San Diego County, California. Xpert MTB/RIF results were compared to acid-fast bacilli (AFB) smear microscopy, mycobacterial culture, and phenotypic drug susceptibility testing (DST). The findings demonstrated that Xpert MTB/RIF is able to accurately detect MTBC and RIF resistance in routinely collected respiratory specimens in a low TB-incidence setting, with comparable performance to that achieved in high-incidence settings; and suggest that under these conditions the assay has particular utility in detecting smear-negative TB cases, excluding smear-positive patients without MTBC disease, and differentiating MTBC from NTM.¹²

CONCLUSION

The GeneXpert MTB/RIF test has significant sensitivity and specificity for the diagnosis of EPTB.

REFERENCES

1. Pai M, Ling DI. 2008. Rapid diagnosis of extrapulmonary tuberculosis using nucleic acid amplification tests: what is the evidence? *Future Microbiol.* 3:1–4.
2. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, Allen J, Tahirli R, Blakemore R, Rustomjee R, Milovic A, Jones M, O'Brien SM, Persing DH, Ruesch-Gerdes S, Gotuzzo E, Rodrigues C, Alland D, Perkins MD. 2010. Rapid molecular detection of tuberculosis and rifampin resistance. *N. Engl. J. Med.* 363:1005–1015.
3. Steingart KR, Schiller I, Horne DJ, Pai M, Boehme CC, Dendukuri N. 2014. Xpert MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults (review). *John Wiley & Sons, Hoboken, NJ.* 10.1002/14651858.CD009593.pub3
4. Lawn SD, Zumla AI. 2012. Diagnosis of extrapulmonary tuberculosis using the Xpert(R) MTB/RIF assay. *Expert Rev. Anti Infect. Ther.* 10:631–635.
5. Tortoli E, Russo C, Piersimoni C, Mazzola E, Dal Monte P, Pascarella M, Borroni E, Mondo A, Piana F, Scarparo C, Coltella L, Lombardi G, Cirillo DM. 2012. Clinical validation of Xpert MTB/RIF for the diagnosis of extrapulmonary tuberculosis. *Eur. Respir. J.* 40:442–447.
6. Centers for Disease Control and Prevention Updated guidelines for the use of nucleic acid amplification tests in the diagnosis of tuberculosis. *MMWR Morb. Mortal. Wkly Rep.* 2009;58:7–10.
7. Lawn SD, Nicol MP. Xpert(R) MTB/RIF assay: development, evaluation and implementation of a new rapid molecular diagnostic for tuberculosis and rifampicin resistance. *Future Microbiol.* 2011;6:1067–1082.
8. Boehme CC, Nabeta P, Hillemann D, et al. Rapid molecular detection of tuberculosis and rifampin resistance. *N. Engl. J. Med.* 2010;363:1005–1015.
9. Tortoli E, Russo C, Piersimoni C, et al. Clinical validation of Xpert MTB/RIF for the diagnosis of extrapulmonary tuberculosis. *Eur. Respir. J.* 2012 doi:10.1183/09031936.00176311
10. Nicol MP, Workman L, Isaacs W, et al. Accuracy of the Xpert MTB/RIF test for the diagnosis of pulmonary tuberculosis in children admitted to hospital in Cape Town, South Africa: a descriptive study. *Lancet Infect. Dis.* 2011;11:819–824
11. Chakravorty S, Simmons AM, Rowneki M, Parmar H, Cao Y, Ryan J, Banada PP, Deshpande S, Shenai S, Gall A, Glass J. The new Xpert MTB/RIF Ultra: improving detection of *Mycobacterium tuberculosis* and resistance to rifampin in an assay suitable for point-of-care testing. *MBio.* 2017 Aug 29;8(4):e00812-17.
12. Rice JP, Seifert M, Moser KS, Rodwell TC. Performance of the Xpert MTB/RIF assay for the diagnosis of pulmonary tuberculosis and rifampin resistance in a low-incidence, high-resource setting. *PLoS one.* 2017 Oct 9;12(10):e0186139.