ORIGINAL ARTICLE

Utility of GeneXpert MTB/RIF in the Rapid Diagnosis of Extra Pulmonary Tuberculosis

Praful S Patil[1], Dhruba H Chandi[2], Ashok Rangaiahagari[3]

Received on: 23 June 2022; *Accepted on:* 12 October 2022; *Published on:* 14 March 2023

Abstract

Introduction: The diagnosis of extrapulmonary tuberculosis (EPTB) is a challenge. World Health Organization (WHO) recommends the use of GeneXpert MTB/RIF assay [Cepheid, United States of America (USA)], using a heminested real-time polymerase chain reaction (PCR) to amplify a *Mycobacterium tuberculosis*-specific sequence of the rpoB gene for the rapid and simultaneous detection of *M. tb* complex (MTBC) and resistance to rifampicin from a clinical specimen. The purpose of this study is to evaluate the performance of the GeneXpert MTB/RIF test with conventional mycobacterial culture in EPTB specimens.

Materials and methods: This prospective study (February–October 2017, 11 months) includes data on 287 EPTB specimens that were processed by conventional culture on Lowenstein–Jensen (LJ) medium and the rapid molecular-based GeneXpert MTB/RIF assay system.

Results: Among the 287 EPTB samples tested, GeneXpert detected the deoxyribonucleic acid of MTBC in 51 samples (17.8%). Standard bacteriological assays, including acid-fast bacilli microscopy and culture, were positive in 26 (9.1%) and 35 (12.1%) specimens respectively. The performance of GeneXpert results was evaluated against culture as a gold standard. The overall sensitivity and specificity of the Xpert assay were calculated to be 94.6 and 94.4%, respectively. The sensitivity of the Xpert assay with tissue specimens was 84.6 and 80.7% specificity, while there was 86.6% sensitivity and 98.1% specificity with the body fluids.

Conclusion: GeneXpert had high performance than culture for the EPTB specimen. It can be a useful tool for the early diagnosis of patients with high clinical suspicion of EPTB. The other major advantage of GeneXpert is that it simultaneously detects rifampicin resistance within 2 hours.

Keywords: Extrapulmonary tuberculosis, GeneXpert MTB/RIF test, Real-time polymerase chain reaction.

Indian Journal of Respiratory Care (2023): 10.5005/jp-journals-11010-1003

Introduction

Tuberculosis (TB) remains a major global health problem. In 2016, WHO notified 6.3 million new TB cases.[1] EPTB comprises a wide spectrum of diseases affecting all parts of the body excluding the lungs. In India 10–15% of cases are EPTB (TB disease). The diagnosis of EPTB is a challenge because of the paucibacillary state and also due to a lack of diagnostic means; they often remain untreated.[2] In the market many commercial tests are available for the diagnosis of TB, but they lack the sensitivities, specificities, and turnaround time is more and unable to detect rifampicin resistance.[3] WHO recommends the use of GeneXpert MTB/RIF assay (Cepheid, USA), using a heminested real-time PCR to amplify a *M. tb*-specific sequence of the rpoB gene for the rapid and simultaneous detection of MTBC and resistance to rifampicin from a clinical specimen. The early detection of *M. tb* and multidrug resistance is a priority in TB diagnosis to improve the successful treatment rate of TB and reduce transmission.[4,5] The purpose of this study is to evaluate the performance of the GeneXpert MTB/RIF test with conventional mycobacterial culture in EPTB specimens.

Materials and Methods

This prospective study was conducted at Credence diagnostic Centre, Moula Ali, Secunderabad, Telangana, from February to October 2017 and approved by the organization Ethical Committee. A total of 287 EPTBs were included in the study. Extrapulmonary samples included cerebrospinal fluid (CSF), pleural fluid, urine, other sterile fluids, lymph node tissue, fine-needle aspirates, and pus samples from various anatomical sites. All samples were processed for Ziehl–Neelsen staining, the GeneXpert MTB/RIF assay, and conventional culture on LJ medium as per standard procedures.[6] Contaminated samples were decontaminated by using NALC–NaOH (N-acetyl-L-cysteine–sodium hydroxide)and the deposit was inoculated in LJ medium. Sterile samples were inoculated directly into the LJ medium.

Nontuberculous *Mycobacterium* was differentiated from MTBC by using a commercially available TBc identification (Becton Dickinson and Company) assay.

[1]Department of Microbiology, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education & Research (DMIHER) (Deemed to be University), Wardha, Maharashtra, India

[2]Department of Microbiology, Datta Meghe Institute of Medical Sciences, Datta Meghe Institute of Higher Education & Research (DMIHER) (Deemed to be University), Wanadongri, Maharashtra, India

[3]Department of Microbiology, Dungarpur Medical College, Dungarpur, Rajasthan, India

Corresponding Author: Ashok Rangaiahagari, Department of Microbiology, Dungarpur Medical College, Dungarpur, Rajasthan, India, e-mail: ashokrnims@yahoo.co.in

How to cite this article: Patil PS, Chandi DH, Rangaiahagari A. Utility of GeneXpert MTB/RIF in the Rapid Diagnosis of Extra Pulmonary Tuberculosis. Indian J Respir Care 2023;12(1):46–48.

Source of support: Nil

Conflict of interest: None

By using culture as a gold standard, the accuracy of the GeneXpert MTB/RIF assay was calculated. The specificity, sensitivity, negative predictive value (NPV), and positive predictive value (PPV) were calculated. Statistical analyses were done by using MedCalc (version 14.8.1, MedCalc software).

Results

A total of 287 samples from different patients were included in the study, repeat samples were excluded. Around 174 samples were body fluid and the remaining 113 samples were tissues, the distribution of samples were shown in Table 1.

As shown in Table 1, 51 samples were positive for GeneXpert MTB, 35 samples grow MTB complex, and only 26 samples were smear positive. Overall performance of the GeneXpert MTB/RIF assay was good with sensitivity of 94.6% and specificity of 94.4% using culture as a gold standard (Table 2).

Discussion

In current days EPTB is a major problem in controlling TB because of the paucibacillary state which is very difficult to detect by conventional methods. GeneXpert MTB/RIF assay offers a substantial advantage for a clinician seeking an early diagnosis in a paucibacillary EPTB sample. The detection of EPTB varies with different specimens by using Xpert.

The current study is to evaluate the performance of the GeneXpert MTB/RIF test with conventional mycobacterial culture in EPTB specimens. The sensitivity and specificity of the current study for Xpert MTB/RIF assay were 83.3 and 100%. The sensitivity and specificity of Xpert MTB/RIF assay from other studies ranged from 58.3 to 85% and 87 to 100%, respectively, which were shown in the Table 3.[7–12]

In the current study, the sensitivity of Xpert MTB/RIF for pus, CSF, and lymph node were 100%, followed by pleural fluid (83.3%) and the lowest was urine 66.6%. The specificity for urine was 100%, followed by pleural fluid (98.8%), CSF (89.3%), and lowest for lymph node (87.5%). Which is similar to Scott et al.,[7] The sensitivity and specificity of Xpert MTB/RIF versus Mycobacteria Growth Indicator Tube culture were 59 and 92%, respectively. Xpert MTB/RIF had the highest sensitivity on pus 91%, followed by aspirates 80% and fluids 51%. The specificity values for Xpert compared to culture were lowest for pus 76% and aspirates 78%. Among the fluids, Xpert MTB/RIF had a higher sensitivity for ascitic fluids 59% than for pleural fluids 47%.

Table 1: Xpert accuracy according to smear and culture results

Specimen	*Total*	*Smear*	*GeneXpert*	*Culture (MTB)*
Fluids (*n* = 174)				
Pleural fluid	89	1	6	5
CSF	30	2	5	2
Pus	17	6	6	4
Urine	13	0	2	2
Pericardial fluid	8	0	0	0
Peri pancreatic fluid	1	0	0	0
Ascitic fluid	9	0	0	0
Bone marrow aspiration	2	0	0	0
Synovial fluid	5	0	0	0
Total	174	9	19	13
Tissues (*n* = 113)				
Lymphnode	64	13	28	22
Breast tissue	11	0	0	0
Endometrial tissue	16	0	1	0
Git tissue	12	2	2	0
Bone tissue	2	0	0	0
Renal tissue	3	2	1	0
Soft (muscle) tissue	5	0	0	0
Total	113	17	32	22

Table 2: Sensitivity and specificity of Xpert in comparison with culture results for EPTB

Stats	*Pleural fluid (N = 89)*	*CSF (N = 30)*	*Urine (N = 13)*	*Lymphnode (N = 64%)*
Sensitivity	83.3%	100%	66.6%	100%
Specificity	98.8%	89.3%	100	87.5%
PPV	83.3%	40%	100	78.6%
NPV	98.8%	100%	91.7%	100%

Table 3: Performance of Xpert MTB/RIF assay for EPTB from various studies

Country	*Study year*	*Nature of specimens*	*Compared with (gold standard)*	*Sensitivity of Xpert/RIF*	*Specificity of Xpert/RIF*
South Africa	Scott et al., 2014[7]	Pus, aspirates, pleural fluids, CSF, tissue, asitic fluids	Liquid culture	59%	92%
India	Bankar et al., 2017[8]	Lymph node	Solid media	85	87
UAE	Habous et al., 2019[9]	Lymph node, aspirates, CSF, gastric lavage, body fluids, pus, urine, and other tissue samples.	Solid and liquid media	83	100
Morocco	Mechal et al., 2019[10]	CSF, tissue biopsies, osteoarticular sampling, pus, pleural fluid or biopsies, urine	Solid and liquid media	79.3	90.3
Iran	Allahyartorkaman et al., 2019[11]	CSF, pericardium, tissue biopsies, osteoarticular sampling, pus, pleural fluid or biopsies, urine	Solid media	77	96
Spain	Moure et al., 2011[12]	Tissue body fluids Aspirates	Solid and liquid media	58.3	100

Conclusion

The result of current study is like the other studies. GeneXpert MTB/RIF assay offers a substantial advantage for a clinician seeking an early diagnosis in a paucibacillary EPTB sample when compare to culture as a gold standard. WHO also recommend the use of XpertMTB/RIFas auseful rapid tool for early diagnosis of patients with high clinical suspicion of EPTB and simultaneously detects rifampicin resistance within 2 hours.

Acknowledgment

We are grateful to our representative institutes for providing the support to complete this work.

Authors' Contributions

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

References

1. "Global tuberculosis report," http://www.who.int/tb/publications/global report/en/,WHO 2017.
2. Solovic I, Jonsson J, Korzeniewska-Kosela M et al. Challenges in diagnosing extrapulmonary tuberculosis in the European Union, 2011. Euro Surveill 2013;18(12):20432. DOI: https://doi.org/10.2807/ese.18.12.20432-en
3. Barnes PF. Rapid diagnostic tests for tuberculosis: progress but no gold standard. Am J Respir Crit Care Med 1997;155(5):1497–1498. DOI: 10.1164/ajrccm.155.5.9154847
4. Vadwai V, Boehme C, Nabeta P, et al. Xpert MTB/RIF: a new pillar in diagnosis of extrapulmonary tuberculosis? J Clin Microbiol 2011;49(7):2540–2545. DOI: 10.1128/JCM.02319-10
5. Rasheed W, Rao N, Adel H, et al. Diagnostic accuracy of Xpert MTB/RIF in sputum smear-negative pulmonary tuberculosis. Cureus 2019;11(8):e5391. DOI: 10.7759/cureus.5391
6. Metaferia Y, Seid A, Fenta GM, et al. Assessment of extrapulmonary tuberculosis using Gene Xpert MTB/RIF assay and fluorescent microscopy and its risk factors at Dessie Referral Hospital, Northeast Ethiopia. Biomed Res Int 2018;2018:8207098. DOI: 10.1155/2018/8207098
7. Scott LE, Beylis N, Nicol M, et al. Diagnostic accuracy of Xpert MTB/RIF for extrapulmonary tuberculosis specimens: establishing a laboratory testing algorithm for South Africa. J Clin Microbiol 2014;52(6):1818–1823. DOI: 10.1128/JCM.03553-13
8. Bankar S, Set R, Sharma D, et al. Diagnostic accuracy of Xpert MTB/RIF assay in extrapulmonary tuberculosis. Indian J Med Microbiol 2018;36(3):357–363. DOI: 10.4103/ijmm.IJMM_18_173
9. Habous M, E Elimam MA, Kumar R, et al. Evaluation of GeneXpert *Mycobacterium tuberculosis*/rifampin for the detection of *Mycobacterium tuberculosis* complex and rifampicin resistance in nonrespiratory clinical specimens. Int J Mycobacteriol 2019;8(2):132–137. DOI: 10.4103/ijmy.ijmy_83_19
10. Mechal Y, Benaissa E, El Mrimar N, et al. Evaluation of GeneXpert MTB/RIF system performances in the diagnosis of extrapulmonary tuberculosis. BMC Infect Dis 2019;19(1):1069. DOI: 10.1186/s12879-019-4687-7
11. Allahyartorkaman M, Mirsaeidi M, Hamzehloo G, et al. Low diagnostic accuracy of Xpert MTB/RIF assay for extrapulmonary tuberculosis: A multicenter surveillance. Sci Rep 2019;9(1):18515. DOI: 10.1038/s41598-019-55112-y
12. Moure R, Martín R, Alcaide F. Effectiveness of an integrated real-time PCR method for detection of the *Mycobacterium tuberculosis* complex in smear-negative extrapulmonary samples in an area of low tuberculosis prevalence. J Clin Microbiol 2012;50(2):513–515. DOI: 10.1128/JCM.06467-11