Utility of genexpert MTB/RIF in the rapid diagnosis of extra pulmonary tuberculosis.

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Abstract

Introduction: The diagnosis of extra pulmonary Tb (EPTB) is a challenge. World Health Organization recommends the use of Genexpert MTB/RIF assay (Cepheid, USA), using a hemi nested real-time PCR to amplify an M. tuberculosis-specific sequence of the rpo B gene for the rapid and simultaneous detection of Mycobacterium tuberculosis complex (MTBC) and resistance to rifampicin from 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 to Oct 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, the genexpert detected the DNA of MTBC in 51 samples (17.8%). Standard bacteriological assays, including AFB microscopy and culture, were positive in 26 (9.1%) and 35 (12.1%) specimens respectively. Performance of genexpert results was evaluated against. 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 performances than culture for EPTB specimen. It can be a useful tool for early diagnosis of patients with high clinical suspicion of EPTB. The other major advantage of Gene Xpert is that it simultaneously detects Rifampicin resistance within 2 hours.

Introduction

Tuberculosis (TB) remains a major global health problem. In 2016, WHO notified 6.3 million new tuberculosis cases [1]. Extra pulmonary tuberculosis (EPTB) comprises a wide spectrum of disease affecting all parts of the body excluding the lungs. In India 10 to 15% cases are extra pulmonary of tuberculosis (TB disease). The diagnosis of extra pulmonary Tb (EPTB) is a challenge because of pauci bacillary 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 tuberculosis, but they lack the sensitivities, specificities, turnaround time is more and also unable to detect rifampicin resistance [3]. World Health Organization recommends the use of Genexpert MTB/RIF assay (Cepheid, USA), using a hemi nested real-time PCR to amplify an Mycobacterium tuberculosis - specific sequence of the rpoB gene for the rapid and simultaneous detection of Mycobacterium tuberculosis complex (MTBC) and resistance to rifampicin from clinical specimen. The early detection of Mycobacterium tuberculosis 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 in Credence diagnostic Center, Moulali, from February to Oct 2017. A total of 287 EPTB were included in the study. Extra pulmonary 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 (ZN) staining, the genexpert MTB/RIF assay and conventional culture on Lowenstein–Jensen media as per standard procedures [6]. Non sterile samples were decontaminated by using NALC-NaOH (N-acetyl-L-cysteine–sodium hydroxide) and the deposit was inoculated in LJ media. Sterile samples were inoculated directly into the LJ media.

Non tuberculosis Mycobacterium (NTM) was differentiated from Mycobacterium tuberculosis complex (MTBC) by using commercially available TBcID (Becton Dickinson and Company) assay. By using culture as a gold standard the accuracy of the genexpert MTB/RIF assay was calculated. The specificity, sensitivity, negative predictive value

(NPV), positive predictive value (PPV) and were calculated. Statistical analyses were done by using Med Calc (version 14.8.1, Medcalc Software).

Results

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

As shown in the 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 gold standard **Table 2**.

Discussion

In current days EPTB is a major problem in controlling tuberculosis because of pauci bacillary 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 pauci bacillary 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 current study for Xpert MTB/RIF assay was 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 [7-12] **Table 3**.

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	83.30%	100%	66.60%	100%
Specificity	98.80%	89.30%	100	87.50%
PPV	83.30%	40%	100	78.60%
NPV	98.80%	100%	91.70%	100%

Table 3. Performance of Xpert MTB/RIF assay for extra pulmonary tuberculosis from various studies.

Country	Study year	Nature of specimens	Compared with (gold standard)	Sensitivity of Xpert/RIF	Specificity of Xpert/RIF	Reference
South Africa	Lesley ES et al, 2014	Pus, aspirates, pleural fluids, CSF, tissue, asitic fluids,	Liquid culture	59%	92%	7
India	Sheetal B et al, 2017	Lymph node	Solid media	85	87	8
UAE	Maya H et al 2019	lymph node, aspirates, CSF, gastric lavage, body fluids, pus, urine, and other tissue samples.	Solid and liquid media	83	100	9
Morocco	Youness M et al, 2019	CSF, tissue biopsies, osteoarticular sampling,	Solid and liquid media	79.3	90.3	10
		pus, pleural fluid or biopsies, urine				
Iran	Mohammadreza A et al, 2019	CSF, Pericardium, tissue biopsies, osteoarticular sampling, pus, pleural fluid or biopsies, urine	Solid media	77	96	11
Spain	Raquel M, et al, 2011	Tissue Body fluids Aspirates	Solid and liquid media	58.3	100	12

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In current study, the sensitivity of Xpert MTB/RIF for Pus, CSF and lymph node were 100%, followed by pleural fluid (83.3%) and 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%). This is similar to Lesley ES et al, [6] the sensitivity and specificity of Xpert MTB/RIF versus MGIT 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 ascetic fluids 59% than for pleural fluids 47%.

Conclusion

The result of current study is similar to the other studies. Genexpert MTB/RIF assay offers a substantial advantage for a clinician seeking an early diagnosis in a pauci bacillary EPTB sample when compares to culture as a gold standard. WHO also recommend the use of Xpert MTB/RIF as a useful rapid tool for early diagnosis of patients with high clinical suspicion of EPTB and simultaneously detects Rifampicin resistance within 2 hours.

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Authors' Contributions

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Conflict of Interest

No conflict of interest

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Ethics Statement

Not applicable

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