

Assessment of Efficacy of Gene Xpert MTB Assay in Rapid Detection of Mycobacterium Tuberculosis in Extrapulmonary Tuberculosis Patients: An Observational Study

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ABSTRACT

Background: Extrapulmonary infection with members of the Mycobacterium tuberculosis complex (MTBC) remains a diagnosis that is often difficult to establish, since the number of bacteria in extrapulmonary specimens is often lower than the number in pulmonary specimens. Hence; the present study was planned for assessing the efficacy of Gene Xpert MTB Assay in Rapid Detection of Mycobacterium Tuberculosis in Extrapulmonary Tuberculosis patients.

Materials & Methods: A total of 250 patients with Extrapulmonary tuberculosis (EPTB) were included in the present study. Only those patients of EPTB were included in which diagnosis was confirmed on the basis of positivity on ZN staining and LJ culture media and clinco-radiologic manifestations. Collection of extrapulmonary samples was done in all in the patients in sterile containers. The samples were sent to the laboratory for evaluation with GeneXpert MTB assay.

Results: Among these 250 patients, GeneXpert MTB assay showed positivity for 84 percent of the cases, while it showed negativity for remaining 16 percent of the cases. The overall

sensitivity of the GeneXpert test was found to be 84 percent; with positive predictive value being 100 percent.

Conclusion: Efficacy of GeneXpert test is significantly high in routine for diagnosis of EPTB.

Key words: Extrapulmonary, GeneXpert, Tuberculosis.

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INTRODUCTION

With an estimated 9 million new cases and 2 million deaths every year, tuberculosis (TB) remains a leading public health problem worldwide. In the majority of cases, the disease affects the lungs, but there are also not negligible numbers of cases (about 15%) with extrapulmonary involvement in low-incidence countries.¹⁻³ Extrapulmonary infection with members of the Mycobacterium tuberculosis complex (MTBC) remains a diagnosis that is often difficult to establish, since the number of bacteria in extrapulmonary specimens is often lower than the number in pulmonary specimens.^{4,5} In recent times, attention has been devoted to new nucleic acid amplification diagnostic technologies, owing to their rapidity, sensitivity, and specificity. The Xpert MTB/RIF assay, which is based on real-time polymerase chain reaction (PCR) analysis of the TB-specific rpoB gene, is an automated molecular diagnostic test for simultaneous detection of mycobacterium tuberculosis (MTB) and rifampin (RIF) resistance directly from clinical specimens. The assay has shown high

sensitivity and specificity.⁶ Hence; the present study was planned for assessing the efficacy of Gene Xpert MTB Assay in Rapid Detection of Mycobacterium Tuberculosis in Extrapulmonary Tuberculosis patients.

MATERIALS & METHODS

The present study was conducted in the Department of TB & Chest, Narayan Medical College, Jamuhar, Sasaram, Bihar (India) and it included assessment of efficacy of Gene Xpert MTB Assay in Rapid Detection of Mycobacterium Tuberculosis in Extrapulmonary Tuberculosis patients.

Ethical approval was obtained from the ethical committee of the institution. A total of 250 patients with EPTB were included in the present study. Only those patients of EPTB were included in which diagnosis was confirmed on the basis of positivity on ZN staining and LJ culture media and clinco-radiologic manifestations. Collection of extrapulmonary samples was done in all in the

patients in sterile containers. The samples were sent to the laboratory for evaluation with GeneXpert MTB assay. All the results were recorded in Microsoft excel sheet and were analysed by SPSS software.

RESULTS

In the present study, analysis of a total of 250 patients was done. Among these 250 patients, 64 percent were males while the

remaining 36 percent were females. 52 percent of the patients belonged to the age group of more than 40 years. In the present study among these 250 patients, GeneXpert MTB assay showed positivity for 84 percent of the cases, while it showed negativity for remaining 16 percent of the cases. In the present study, the overall sensitivity of the GeneXpert test was found to be 84 percent; with positive predictive value being 100 percent.

Graph 1: Age-wise and gender-wise distribution of patients

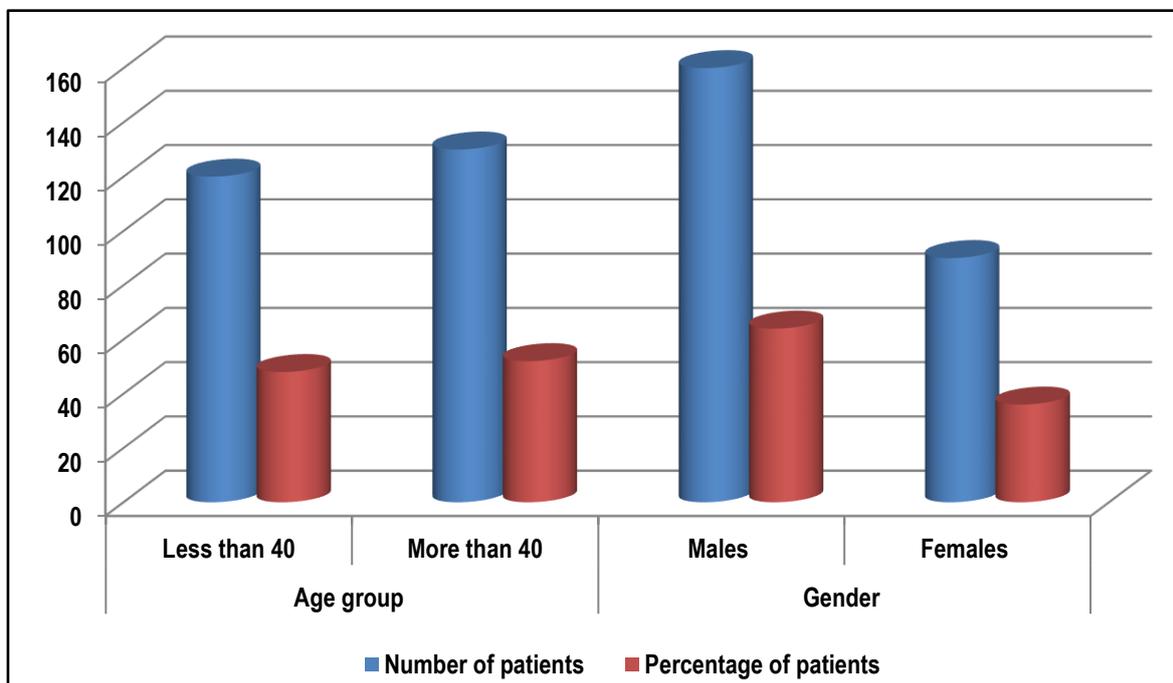


Table 1: Results of GENE XPRT MTB assay

Parameter	Number of patients	Percentage
Positive	210	84
Negative	40	16
Total	250	100

Table 2: Overall sensitivity of GENE XPRT MTB in the detection extra-pulmonary tuberculosis patients

Parameter	Value	95% CI
Sensitivity	84%	78.86% to 88.32%
Specificity	-	-
Positive predictive value	100%	-
Negative predictive value	0%	-
Accuracy	84%	78.86% to 88.32%

DISCUSSION

Tuberculosis remains a major public health problem globally, with India being one of the high burden countries. The common causative agent is Mycobacterium tuberculosis but in developing countries M. bovis is reported as a potential human pathogen. Almost 20% of all reported cases of tuberculosis are of extra pulmonary form of disease. Diagnosis of extra pulmonary tuberculosis (EPTB) is not always possible with conventional

methods, due to the long time required and the paucibacillary nature of samples; hence the need of rapid molecular methods.^{7,8} Molecular techniques have substantially changed the field of tuberculosis diagnosis and have been proven to yield rapid results while being highly sensitive. Numerous PCR assays employing a number of different M. tuberculosis targets have recently been described. The new Xpert assay tested in our study targets the rifampin resistance-associated rpoB gene region by heminested

PCR with three specific primers and combines the sensitive detection of *M. tuberculosis* DNA and determination of RMP resistance.⁹

In the present study, analysis of a total of 250 patients was done. Among these 250 patients, 64 percent were males while the remaining 36 percent were females. 52 percent of the patients belonged to the age group of more than 40 years. Extrapulmonary sites of infection commonly include lymph nodes, pleura, and osteoarticular areas, although any organ can be involved. The diagnosis of extrapulmonary tuberculosis can be elusive, necessitating a high index of suspicion. Physicians should obtain a thorough history focusing on risk behaviors for human immunodeficiency virus (HIV) infection and tuberculosis. Antituberculous therapy can minimize morbidity and mortality but may need to be initiated empirically. A negative smear for acid-fast bacillus, a lack of granulomas on histopathology, and failure to culture *Mycobacterium tuberculosis* do not exclude the diagnosis. Novel diagnostic modalities such as adenosine deaminase levels and polymerase chain reaction can be useful in certain forms of extrapulmonary tuberculosis.^{9, 10}

In the present study among these 250 patients, GeneXpert MTB assay showed positivity for 84 percent of the cases, while it showed negativity for remaining 16 percent of the cases. The Xpert MTB/RIF assay is an automated nucleic acid amplification test for clinical specimens that can identify MTB and resistance to RIF with minimal labor. When tested in areas with high TB incidence, the Xpert assay was highly accurate, with a sensitivity of 88% and specificity of 98%. In Korea, the sensitivity and specificity of the Xpert assay for the diagnosis of pulmonary TB were reported to be 79.5% and 100%, respectively.^{11- 12}

In the present study, the overall sensitivity of the GeneXpert test was found to be 84 percent; with positive predictive value being 100 percent. There are a large number of studies evaluating Xpert on pulmonary specimens; the sensitivity varies from 95% to 100% in smear-positive sputa, and from 47% to 77% in smear-negative ones. The diagnosis of TB, and especially of EPTB, is based on the combination of multiple tests; among them, the main role of the culture is once more confirmed with the potential of Xpert being high in ruling in, but suboptimal in ruling out, EPTB. Among the rapid tests investigated here, Xpert's sensitivity scored twice as high in comparison with microscopy thus doubling the proportion of rapid diagnoses, with important rebound on the patients' outcome.^{10- 12}

CONCLUSION

From the above results the authors conclude that efficacy of GeneXpert test is significantly high in routine for diagnosis of extrapulmonary TB. However; further studies are recommended.

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