Usefulness of GeneXpert MTB/RIF in the diagnosis of extra-pulmonary tuberculosis

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ABSTRACT

Background: Diagnosis of extra-pulmonary tuberculosis (TB) is often delayed because of diverse clinical presentations and difficulties in establishing the bacteriological diagnosis. This study aimed to evaluate usefulness of GeneXpert MTB/RIF in the diagnosis of extra-pulmonary TB in Bangladeshi patients.

Methods: This cross-sectional study was done in BIRDEM General Hospital, Dhaka, Bangladesh from 2013 to 2016 as a part of Bangladesh Diabetic Somiti (BADAS)-USAID-TB Care-II project. Representative samples from 590 clinically suspected extra-pulmonary TB cases were tested for GeneXpert MTB/RIF along with conventional methods.

Results: Total patients were 590 [mean age 43.9 (range 1-95) years] with male predominance (326, 55.3%). Most (513, 86.9%) patients were diabetic and new (574, 97.3%) TB suspects; while 16 (2.7%) patients had past history of TB. Common samples were pleural fluid (125, 21.2%), urine (110, 18.6%), cerebrospinal fluid (CSF) (91, 15.4%), pus (82, 13.9%), tracheal aspirates (57, 9.7%), ascitic fluid (45, 7.6%), gastric lavage (31, 5.3%), broncho-alveolar lavage (BAL) (18, 3.1%), lymph node aspirates (11, 1.9%) and synovial fluid (8, 1.4%). Among 590 samples, 68 (11.5%) were positive for Mycobacterium tuberculosis. Diagnostic yield was common for lymph nodes (4/7, 57.1%), pus (25/82, 30.5%), BAL (4/18, 22.2%), tracheal aspirates (8/57, 14.0%), urine (7/110, 6.4%), CSF (6/91, 6.6%) and pleural fluid (7/125, 5.6%). Of the 68 GeneXpert MTB/RIF positive samples, 52 (76.1%) were rifampicin sensitive, 16 (23.9%) showed intermediate sensitivity and none of the samples was resistant to rifampicin.

Conclusions: GeneXpert MTB/RIF appeared as useful tool for diagnosing extra-pulmonary TB.

Key words: Extra-pulmonary tuberculosis, GeneXpert MTB/RIF, usefulness.

Introduction

Tuberculosis (TB) is an ancient disease and it continues to be a major public health problem throughout the world. Poverty, malnutrition, high population density and poor health care facility remain as the predominant causes for TB in low- and middle-income countries, while human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS), malignancy, chemotherapy and use of immunosuppressive drugs come at the top of list as causes for TB infection and TB disease in developed countries.1-3 Bangladesh is one of the high TB burden countries in the world and also drug resistant TB cases.4 About one-fifth of all TB cases are extra-pulmonary TB throughout the world, which may reach up to 42%, specially in children.5 Extra-pulmonary TB poses significant challenges in establishing the diagnosis; the clinical presentation is diverse, there is lack of definitive
diagnostic tools, unavailability of diagnostic facilities, long time requirement for culture of samples, etc.  
 Considering all these shortcomings, GeneXpert MTB/ RIF is considered as an important tool in establishing the diagnosis and identifying rifampicin resistance in TB cases. This study was designed to evaluate the utility of GeneXpert MTB/RIF in the diagnosis of extra-pulmonary TB.

**METHODS**

This cross-sectional study was done in Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh over a period of four years, from 2013 to 2016, as a part of Bangladesh Diabetic Somiti (BADAS)-USAID-TB Care-II project. Representative samples from 590 clinically suspected TB cases, irrespective of age and sex, were tested for GeneXpert MTB/RIF along with conventional methods.

**RESULTS**

Total patients were 590 (mean age 43.9 years) with male predominance (55.3%). Most (513, 86.9%) patients were diabetic and new (574, 97.3%) TB suspect. Base-line characteristics are shown in Table I. Common samples were pleural fluid (125, 21.2%), urine (110, 18.6%), cerebrospinal fluid (CSF) (91, 15.4%) and pus (82, 13.9%). Others are shown in Table II.

Among 590 samples, 68 (11.5%) were positive for *Mycobacterium tuberculosis*. Diagnostic yield was common for lymph nodes (4/7, 57.1%), pus (25/82, 30.5%), Broncho-alveolar lavage (BAL) (4/18, 22.2%) and tracheal aspirates (8/57, 14.0%). Others are shown in Table III. Of the 68 GeneXpert MTB/RIF positive samples, 52 (76.1%) were rifampicin sensitive, 16 (23.9%) showed intermediate sensitivity and none of the samples was resistant to rifampicin.

**DISCUSSION**

Extra-pulmonary TB poses a serious health issue, in terms of morbidity and mortality and health care related costs. Up to one-fifth of TB cases are extra-pulmonary TB. Frequency varies depending up on geographic distribution, TB endemicity, HIV status and available health care facility.  

Extra-pulmonary TB cases are often late to diagnosis. Symptom of extra-pulmonary TB are non-specific and somewhat depend on site of involvement. Clinical findings are also non-specific. Diagnostic facilities like identification of *M. tuberculosis* in smear or culture are difficult, because of various reasons; inadequate sampling, paucibacillary infections, etc. Acid fast bacilli (AFB) cultures require longer times for growth and thus reporting. Histopathological findings can mimic
granulomatous inflammation with a wide range of differentials including TB, fungal infections, sarcoidosis, etc.

Gene Xpert MTB/RIF is an efficient tool, recommended by the World Health Organization for the identification of MTB and rifampicin resistance.\textsuperscript{9,11} It takes 2 hours for the processing and reporting.\textsuperscript{12} In different reports, it has been established that most RIF-resistant TB cases identified by GeneXpert MTB/RIF are also multi-drug resistant TB cases.\textsuperscript{13} So, utility of GeneXpert in diagnosing and identifying rifampicin resistance is well established.

In our study, most samples of extra-pulmonary sites were pleural effusion, urine, CSF and pus and diagnostic yields were most common for lymph nodes and pus. Overall 11.5\% cases were detected by GeneXpert MTB/RIF in the current study and none of the patients showed rifampicin resistance. In a study done in Morocco, extra-pulmonary TB was diagnosed by GeneXpert MTB/RIF assay in 18.41\% cases with 0.84\% cases of rifampicin resistance.\textsuperscript{10}

Regarding GeneXpert MTB/RIF positivity, lymph nodes and pus were in two-thirds and one-third of cases respectively in our study. Mechal Y et al in their study found that the sensitivity of GeneXpert MTB/RIF was highest in osteo-articular samples, followed by pus and lymph nodes.\textsuperscript{10} In a study done in Tunisia, 77\% of lymph node TB cases were identified by GeneXpert MTB/RIF assay.\textsuperscript{14} In a multi-center Italian study, the sensitivity and specificity of GeneXpert MTB/RIF for extra-pulmonary TB was 79\% and 97.3\% respectively when compared with culture results.\textsuperscript{15} Two Pakistani series identified 37\% and 45.3\% extra-pulmonary TB cases by GeneXpert MTB/RIF assay.\textsuperscript{16} An Indian study reported 18.1\% cases of GeneXpert MTB/RIF positivity from extra-pulmonary samples with 2.73\% rifampicin resistance.\textsuperscript{17}

**Limitations of the study**

We could not evaluate our cases against standard microscopic examinations and mycobacterial cultures. It was a single center study with small numbers of study participants.

**Conclusion**

Gene Xpert MTB/RIF appeared to be a useful tool for diagnosing extra-pulmonary TB, specially for pus and pleural effusions and we did not find any rifampicin resistant case. Early detection and treatment definitely reduce the burden and the possibility of developing drug resistance, where the Gene Xpert plays the vital role and might be used whenever possible for a better patient outcome.

**Authors' contribution:** NI planned the research. MDH was overall supervisor. MAR drafted manuscript. JUA, MKA, FA were involved in different stages of the research. All authors read and approved the final manuscript for submission.

**Conflict of interest:** Nothing to declare.

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**REFERENCES**


