

RAPID DETECTION OF TUBERCULOSIS AND RIFAMPICIN RESISTANCE WITH AUTOMATED GENEXPERT MTB/RIF ASSAY

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ABSTRACT

Objective: To Determine the Sensitivity and specificity of GeneXpert Test for diagnosis of Tuberculosis and Rapid detection of Rifampicin Resistance in Smear Positive and Smear Negative Pulmonary Tuberculosis cases.

Background and Methods: Mycobacterium Tuberculosis (TB) is a Major health problem across the world and currently killing 1.5 million people every year. The early detection of Tuberculosis is essential to reduce the death rate and interrupt the transmission. The GeneXpert MTB/RIF test is the novel integrated diagnostic device for the diagnosis of Tuberculosis and rapid detection of Rifampicin resistance, which can lead to Tuberculosis detection in a less than 02 hours. This study is a prospective and conducted between December, 2011 to March, 2014 at PMDT Site, Department of Pulmonology, Chandka Medical College, Shaeed Mohtarma Benazir Bhutto Medical University.

Results: Among the total 2019 patients, 1210 were Sputum Smear Positive & 809 were Sputum Smear Negative. The overall sensitivity was 91.15% and specificity was 100% for the diagnosis of Pulmonary Tuberculosis Smear +ve & Smear -ve cases. The GeneXpert identified 273 cases Rifampicin resistant, 253 were for Sputum Smear +ve and 20 from Sputum Smear -ve pulmonary cases.

Conclusion: The Xpert MTB/RIF is highly sensitive for detection of tuberculosis and Rifampicin resistance. It require reduced time for detection of tuberculosis and Rifampicin resistance compared to the convenience test, that in turn help to initiate timely diagnosis and start of treatment.

Key Words: Genxpert MTB/Assay; Molucular Method; Rifampicin Resistant; Rapid Detection of TB

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INTRODUCTION

Tuberculosis is one of the greatest killers in world due to infection and it accounts more than 1.4 million deaths during 2011. It is a challenge to tackle prevention, diagnosis and the treatment of Tuberculosis due to two complicated factors HIV/AIDS associated TB and Multidrug resistance tuberculosis. The delayed diagnosis is the main factor that leads to death due to late initiation of treatment. Around 8.6 million people worldwide live with a deadly

disease Tuberculosis. Approximately 6 million are still hidden and not on treatment until. Total 300,000 peoples are multi drug resistance. This inference is attributed to late diagnosis and late initiation of treatment of drug sensitive or resistance Tuberculosis either.¹ The Proportion of multidrug resistant Tuberculosis in new cases is 2.9% and in previously treated cases is 15.5% and among the all Tuberculosis cases 4.9%.² In Pakistan total MDR prevalence in new cases is 4.3% while in Re-treatment cases it is 19.4%.³ Mycobacterial culture is the gold standard and most

sensitive method for tuberculosis diagnosis, but it is slow, may take up to 2–8 weeks and expensive.^{4,5} The Smear microscopy for Acid Fast Bacilli is rapid & in expensive it has poor sensitivity and poor positive predictive value. Thus early diagnosis and prompt treatment of TB are crucial to reduce morbidity and mortality. Secondary drug and transmission of Tuberculosis.⁶ In 2011 WHO introduced Xpert MTB/RIF assay and fully automated diagnostic molecular test, using real time polymerase chain (PCR) technology for detection of Mycobacterium Tuberculosis and resistance. Simultaneously the assay can generally be complied in less than 02 hours.^{7,8}

METHODOLOGY

We conducted as hospital based prospective study at Programmatic Management of Drug Resistant TB (PMDT) Site, Department of Pulmonology Chandka Medical College/ Shaheed Mohtarma Benazir Bhutto Medical University, Larkana between 23-12-2011 to 31-02-2014 to determine the sensitivity and specificity of MTB/RIF Assay Test for diagnosis of Tuberculosis and rapid detection of Rifampicin Resistant in Sputum Smear Positive and Sputum Smear Negative Specimen. The patients were divided into two groups One Sputum Smear Positive Pulmonary cases and Second Sputum Smear Negative pulmonary cases.

The inclusion criteria were:

1. Retreatment PTB Cases
 - o All Smear positive and Smear Negative TB patient with the history of previous treatment.
2. New PTB Cases:
 - o Symptomatic contacts of known DR-TB cases.
 - o New PTB cases who are reported Smear Positive at the end of intensive phase.
3. Presumptive TB Cases in Vulnerable Population:
 - o Health care workers (including Laboratory Workers)
 - o PLWHA (People living with HIV)

- o Immune Compromised / Hospitalized or seriously ill.

The eligible patients were asked to provide Sputum specimen. The sputum acid fast smear was performed on ZN Microscopy at PMDT Site Larkana. After than same sample was used for GeneXpert MTB/RIF Assay testing at PMDT Site CMCH Larkana. The Children below 15 year and Extra Pulmonary case were not included in this study.

DATA ANALYSIS

The data entered on Statistical Package for Social Sciences (SPSS 16.0) Version. The data analyzed and the percentage calculated for each variable on mean standard deviation. Chi square test used to analyze to see the relationship of these variables, association considered on (p value<0.05).

RESULTS

A total of 2019 patients, 1117 male and 902 female (Mean age 35 - 45 years) were included in this study. Out of total specimen 1210 sputum Smear Positive and 809 was Smear Negative. The GeneXpert test detected 1264 from them 1210 from Sputum Smear Positive and 54 from Sputum Smear Negative pulmonary cases. According to the result the overall sensitivity of MTB/RIF test was 91.15% and Specificity was 100% the negative predictive value was 88.31% and positive predictive value was 100% as shown in Table No.01. The MTB/RIF test detected 273 RIF Resistant 253 were from Sputum Smear Positive and 20 Sputum Smear Negative Specimen as shown in Fig No.01.

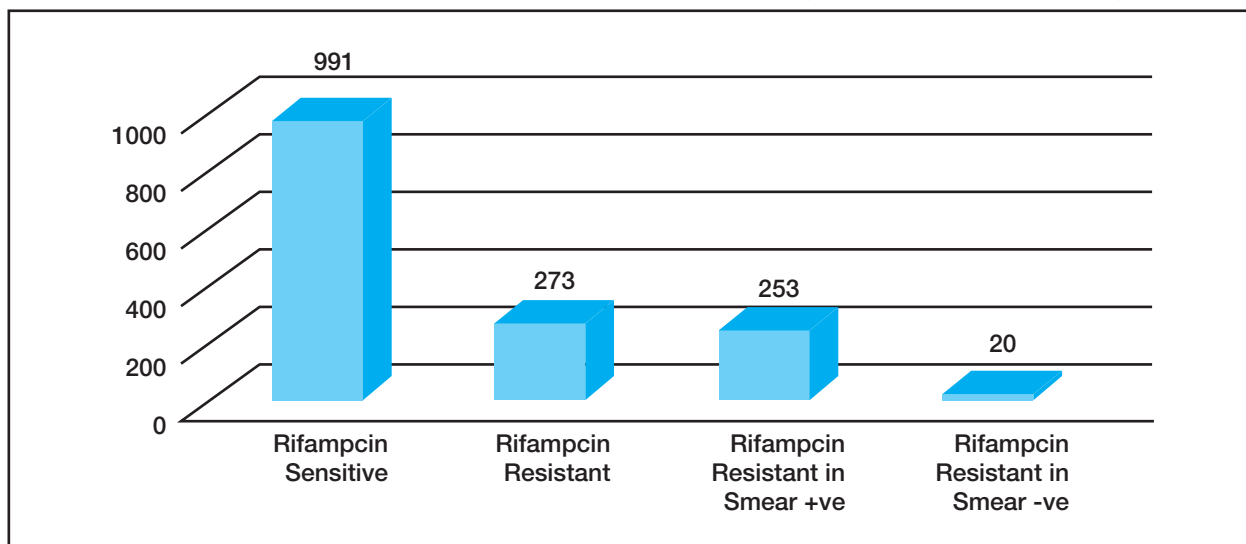
DISCUSSION

One of the most significant steps in tuberculosis control is the fast and accurate disease diagnosis which leads to faster treatment and faster disease control. In this study we determine the sensitivity and specificity of GeneXpert assay for the diagnosis of Tuberculosis and rapid detection of Rifampicin resistant in Smear Positive & Smear Negative pulmonary specimen. This assay identified 1264 cases of Tuberculosis from sputum smear positive 100% (1210/1210) and 67% (54/809) in sputum negative

Table 1: Sensitivity and Specificity of GeneXpert MTB/RIF and Smear for detection of Tuberculosis.

TEST OR METHOD	SENSITI VITY	SPECIFICITY	POSITIVE PREDICTIVE VALUE	NEGATIVE PREDICTIVE VALUE
MTB/RIF ASSAY	91.15%	100%	100%	88.31%
SMEAR	86.69%	98.6%	88.9%	83.40%

Figure 1: Detection of Rifampicin Resistant and Rifampicin Sensitive by Genexpert MTB/RIF Assay n=1264



specimen. Some studies of GeneXpert MTB/RIF assay have reported sensitivity in cases of Smear & Culture positive were 98 - 100% while in cases of Smear Negative and Culture positive were 57 to 76.9% while the test specificity remain 99 to 100% 8, 9, 10, 11, 12. In our studies overall sensitivity in Smear Positive and Smear negative cases were 91.15 % and specificity were 100%. The sensitivity of our study were slightly lower and specificity remain same than those with the other studies.

CONCLUSION

The Xpert MTB/RIF is highly sensitive for detection of tuberculosis and Rifampicin resistance. It require reduced time for detection of tuberculosis and Rifampicin resistance compared to the convenience test, that in turn help to initiate timely diagnosis and start of treatment.

RECOMMENDATIONS

Provision of gene expert machine at every tertiary and if possible at Tehsil level care hospital, with improves the skill of health worker to use the machine that requires less technique. In addition, improve Infrastructure and Electricity problem in consideration.

REFERENCES

1. Jacob Creswell, Andrew J Codin, Emmanuel Andrew, Mark A Mick, Ahmed Bedru, E Jane Carter, Rajendra Parsad Yadavndrei, Mos.
2. Tuberculosis Service. Tuberculosis report in Turkey Ministry of Health Ankara, Turkey 2009.
3. National Guidelines for the Management of the

Drug resistance Tuberculosis DR-TB management; 2014.

4. Van Kampen SC, Anthony RM, Klatser PR. The realistic performance achievable with mycobacterial automated culture systems in high and low prevalence settings. *BMC Infectious Disease* 2010; 10(1):1.
5. Siddiqi K, Lambert ML, Walley J. Clinical diagnosis of smear negative pulmonary tuberculosis in low income countrie: the current evidence. *Lacent Infectious Disease* 2003; 3(5):288-96.
6. Centers for Disease Control and Prevention (CDC). Updated guidelines for the use of nucleic acid amplification tests in the diagnosis of tuberculosis. *MMWR. Morbidity and mortality weekly report.* 2009;58(1):7.
7. Balkemore, R, Story E, Helb D, Kop J, Banada P, Owens MR, et al. Evaluation of the analytical performance of the Xpert MTB/RIF assay. *J. Cin, Micorbiol* 2010; 48: 1772-76.
8. Helb, D, Jones M, Story E, Boehme C, Wallace E, Ho K, et al. Rapid detection of Mycobacterium tuberculosis and Rifampicin resistant by use of on-demand, near patient technology. *J Clin Micorbiol* 2010; 48(1): 229-37.
9. Armand S, Vanhuls P, Delcroix G, Courcol R, Lemaître N. Comparison of the Xpert MTB/RIF test with an IS6110-TaqMan real-time PCR assay for direct detection of Mycobacterium tuberculosis in respiratory and non-respiratory specimen. *J. Clin Microbiol* 2011; 49(5):1772-6.

10. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, et al. Rapid molecular detection of tuberculosis and Rifampicin resistant. *N. Engl. J. Med* 2010; 363(11): 1005-15.
11. Boehme CC, Nicol MP, Nabeta P, Michael JS, Gotuzzo E, Tahirli R et al. Feasibility, diagnosis accuracy, and effectiveness of decentralized use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance; a multicenter implementation study. *Lancet* 2010; 377: 1495-505.
12. Marlowe EM, Novak-Weekley SM, Cumpio J, Sharp SE, Momeny MA, Babst A. et al. Evaluation of the Cepheid Xpert MTB/RIF assay for direct detection of *Mycobacterium tuberculosis* complex in respiratory specimen. *J. Clin. Microbiol* 2011; 49: 1621-3.