

ROLE OF CBNAAT IN RAPID DETECTION OF MYCOBACTERIUM TUBERCULOSIS IN PLHIV IN A HIGHLY PREVALENT STATE

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ABSTRACT

Tuberculosis can occur at any stage of HIV disease and it presents differently according to level of immunosuppression. Patients are paucibacillary, involve hilar and mediastinal lymph nodes, lack cavitation and are smear negative. Sputum culture takes 4-8 weeks for mycobacteria to grow, hence a newly launched cartridge based nucleic acid amplification test by WHO offers a promising solution to these challenges in detecting presumptive pulmonary tuberculosis.

AIM OF STUDY

Comparing efficacy of fluorescent microscopy and CBNAAT for diagnosing pulmonary tuberculosis in PLHIV and detecting Rifampicin resistance.

MATERIAL AND METHODS

This study included all HIV infected patients suspected to have tuberculosis, including drug-resistant tuberculosis, coming to our district tuberculosis centre. The patients were enrolled and provided Xpert MTB/RIF. Simultaneously, smear for AFB was done in same patients.

RESULTS

The study was done for 2 months from February to March 2016. Out of 231 HIV positive patients, 59 cases (25.54%) had tuberculosis. Sputum smear for AFB negative and GeneXpert positive were 45(76.27%). 8(13.55%) cases were Rifampicin resistance and 51 (86.44%) were sensitive out of all tuberculosis patients.

CONCLUSION

This study demonstrates the limitations of conventional sputum microscopy. CBNAAT detects more tuberculosis cases in lesser time. Rifampicin resistance is also detected. Hence drug-resistant tuberculosis can be screened. Early treatment of tuberculosis can be addressed with Xpert MTB/RIF testing.

KEYWORDS

Tuberculosis HIV coinfection, CBNAAT, Drug-resistant Tuberculosis.

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INTRODUCTION: An estimated incidence of 200,000-250,000 HIV-positive TB cases present in India in 2014.⁽¹⁾ India has the world's highest burden of tuberculosis (TB) and third largest number of people living with HIV in the world; and bears the third highest burden of HIV-associated TB in the world. 25,000 to 38,000 patients die each year with this coinfection.⁽¹⁾ While TB is endemic across India, the HIV epidemic is concentrated in six out of 35 states and union territories in the country: Andhra Pradesh, Karnataka, Maharashtra, Tamil Nadu, Manipur and Nagaland. The four largest states of the six (Andhra Pradesh, Karnataka, Maharashtra and Tamil Nadu) currently carry 53% of total burden, but some of the low HIV prevalence states now show rising trends and these increasingly drive the HIV epidemic in India.

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Tuberculosis is most common opportunistic infection. But in a backdrop of sputum smear negative cases other diseases like Pneumocystis jirovecii, Gram-negative bacteraemia and Kaposi sarcoma has to be considered. One third of HIV-TB cases have normal chest X-ray, hence goes underdiagnosed.⁽²⁾ While cheap and relatively easy to perform, fluorescence microscopy, reports of sensitivity range between 59.7% to 83% and that of specificity from 85.5% to 99%^(3,4) cannot differentiate between drug-sensitive and drug-resistant Mycobacterium tuberculosis. The sensitivity of smear microscopy is especially poor in HIV-infected individuals and children.⁽⁵⁾ Culture of sputum for mycobacterial tuberculosis is available only after 2-8 weeks.

Xpert MTB/RIF, holds promising solution by detecting 99% of smear-positive patients and >80% of patients with smear-negative disease. The sensitivity of microscopy has decreased in HIV/TB coinfection, but did not significantly affect Xpert MTB/RIF performance. Rifampicin resistance was detected with 95.1% sensitivity and 98.4% specificity.⁽⁶⁾ The WHO evidence synthesis process confirmed a solid

evidence base to support widespread use of Xpert MTB-RIF for detection of TB and rifampicin resistance. It is therefore recommended that:

1. Xpert MTB/RIF should be used as the initial diagnostic test in individuals suspected of MDR-TB or HIV-associated TB (Strong Recommendation).
2. Xpert MTB/RIF may be used as a follow-on test to microscopy in settings where MDR and / or HIV are of lesser concern, especially in smear-negative specimens (Conditional Recommendation, Recognising Major Resource Implications).

Hence, we have taken up the study of comparing detection of mycobacterial tuberculosis bacilli in sputum by Xpert/RIF and fluorescent smear method in pulmonary tuberculosis and rifampicin resistance with special focus on PLHIV.

MATERIAL AND METHODS: A total of 231 sputum samples which were received by District Tuberculosis Centre, Guntur of all PLHIV patients, who were presumptive tuberculosis cases was collected. Patient details like name, address, age, sex were noted. Two Sputum samples were collected for each patient, in 2 sterile containers. One was sent to our medical college for AFB smear by fluorescent microscopy. Another was diluted with three times the reagent, incubated at room temperature and loaded into the Xpert MTB/RIF cartridge for automated analysis. The following results are obtained: no TB, TB detected, Rifampicin resistance detected, No Rifampicin resistance detected, invalid, indeterminate. Results were obtained in 2 hours.

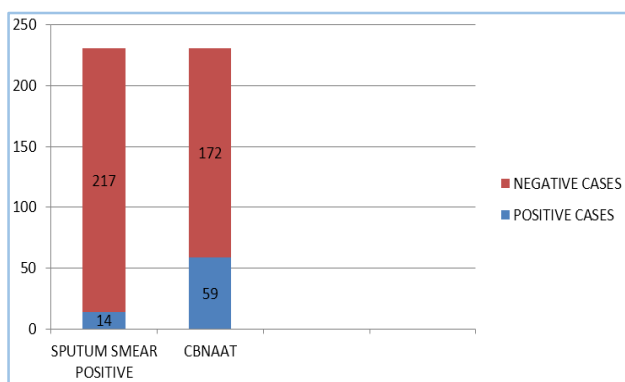


Fig. 1: Total Sputum Smear Confirmed and CBNAAT Confirmed Cases

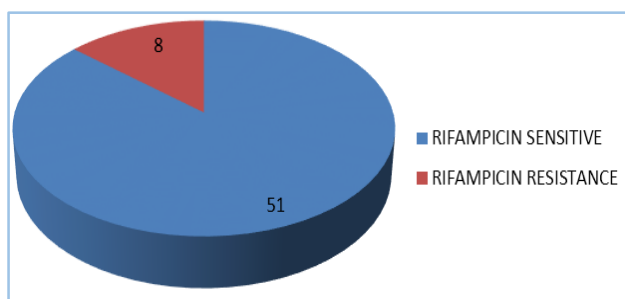


Fig. 2: Rifampicin Sensitive and Rifampicin Resistance in CBNAAT Positive Cases

DISCUSSION: In our study, 145(62.77%) were males and 86(37.23%) were females. In another similar study, done by Sharma SK et al, 583 patients had HIVTB coinfection, out of which 81.3% males and 18.7% female.⁽⁷⁾ Male predominance might be due to migration for employment and their risk behaviour. Females being illiterate are unaware of disease per se.

Since the discovery of tubercle bacilli in 1882, microscopic detection has been a standard test. Advantage of this test is, it is inexpensive, rapid and specific. 10⁽⁵⁾ mycobacteria per millilitre is required for its positivity. Sensitivity in HIV infection ranges from 43% to 51%.⁽⁸⁾ Cattamanchi et al. In our study sensitivity was 23.7% by fluorescence microscopy. Since these patients are paucibacillary, detection is delayed. Hence mortality increases due to delay in initiating antitubercular treatment.⁽⁹⁾

WHO introduced Xpert MTB/RIF in India in 2012 which outperformed smear microscopy. In a high HIV prevalence setting, it diagnosed 47% of smear negative TB cases in a study done by Grant Thereon et al.⁽¹⁰⁾ Our state being a high prevalence area, we had a result of 27.18%. Another study was done in Hyderabad in 2011, detecting 10.8% more cases by CBNAAT over fluorescence microscopy.⁽¹¹⁾

In our study, out of 59 CBNAAT positive cases 8(13.55%) were detected as Rifampicin resistant cases. In a study done by Sethi et al at PGIMER, Chandigarh suggested high prevalence (27.3%) in HIV positive cases, culture was done by LJ media.⁽¹²⁾ WHO global report on Tuberculosis 2013, detected 15.8% MDR-TB in HIV positive cases.

Advantage of GeneXpert is, it is mycobacterium tuberculosis specific, no cross reaction with non-tubercular mycobacteria occurs. Another important aspect is simultaneous detection of rifampicin resistance in 2 hours which in turn helps rapid initiation of MDR treatment.

Major disadvantage is the cost in an underdeveloped country like ours. A study on previously treated tuberculosis showed false positivity of CBNAAT due to dead bacilli.⁽¹³⁾ Other limitations are inability to detect Isoniazid and other drug resistance, continuous electrical supply is required, ambient temperature, dedicated trained personal, annual calibration of the instrument and biosafety precautions.

RESULTS: Tuberculosis was positive in 59 cases out of 231 HIV positive patients (25.54%). Gene Xpert positive and sputum smear for AFB negative cases were 45 (76.27%). Out of 59 CBNAAT positive cases rifampicin resistant cases were 8(13.55%).

CONCLUSION: CBNAAT/RIF can be used as initial test in detecting Tuberculosis in PLHIV, because of its rapidity and detection of Rifampicin resistance.⁽¹⁴⁾ Although sputum should be sent for DST to rule out other drugs resistance. This ultimately will lead to early treatment and reduced mortality.

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