ABSTRACT
Objective: Tuberculosis (TB) is one of the commonest opportunistic infection and the leading cause of death in HIV positive patients. HIV infection is a well recognised risk factor for both activation of initial infection and reactivation of latent infection. This study was done to find out the co-prevalence and the trend of HIV infection among tuberculosis patients and to determine the prevalence of MDR Tuberculosis in HIV positive patients using Xpert MTB/RIF assay (Cepheid, Sunnyvale, CA, United States). Materials and Methods: The sputum samples are received from Indore M.P. India. Sputum samples of the patients with symptoms suggestive of pulmonary tuberculosis including both new cases and on treatment are received from the various DMCs and hospitals. Sputum specimen was processed for TB detection by Cartridge Based Nucleic Acid Amplification testing (CB-NAAT) using Xpert MTB/RiF assay technology. Results: The study period is from 2015 to August 2016. A total of 4595 patients with symptoms suggestive of pulmonary tuberculosis including both new cases and on treatment. Out of these patients 1087 were reported MTB detected. Out of these 4595 patients 953 were reported HIV positive and out of 953 patients 127(13.3%) cases were showing resistance to rifampicin (RIF) Drug. Conclusion: Co-existence of HIV and tuberculosis is high and there is high Prevalence of MDR tuberculosis in HIV patients.

KEYWORDS: Co-infection, Cartridge based nucleic acid amplification testing, Human immunodeficiency virus (HIV), Pulmonary, Rifampicin, Tuberculosis.

INTRODUCTION
Human immunodeficiency virus (HIV) associated tuberculosis (TB) remains a major global public health challenge, with an estimated 1.4 million patients worldwide. Co-infection with HIV leads to challenges in both the diagnosis and treatment of tuberculosis. Further, there has been an increase ingrates of drug resistant tuberculosis, including multi-drug (MDR-TB) and extensively drug resistant TB (XDR-TB), which are difficult to treat and contribute to increased mortality. Because of the poor performance of sputum smear microscopy in HIV-infected patients, newer diagnostic tests are urgently required that are not only sensitive and specific but easy to use in remote and resource-constrained settings.¹

In the global tuberculosis report (2015), WHO reported that in 2014, Worldwide, 9.6 million people are estimated to have fallen ill with TB in 2014: 5.4 million men, 3.2 million women and 1.0 million children. Globally, 12% of the 9.6 million new TB cases in 2014 were HIV-positive. 9 million people developed TB, including 1.1 million cases among people who were HIV positive. At the same time, global burden of multidrug-resistant TB (MDR-TB) was estimated to be 480,000 cases leading to estimated 210,000 deaths.²

HIV and Mycobacterium tuberculosis have a synergistic interaction; each accentuates progression of the other. Clinical presentation of TB in early HIV infection
TB detection was done by Xpert MTB/RIF assay, made by Cepheid-Sunnyvale-USA. Sputum specimens were processed according to the GeneXpert Dx system operator manual given by Central TB division, Government of India, Guidance document for use of cartridge based nucleic acid amplification test (CB-NAAT) under RNTCP. The assay is designed for extraction, amplification and identification of rpoB gene of *M. tuberculosis* as it accounts for more than 95% of mutations associated with rifampicin resistance), ensuring high degree of specificity by use of three specific primers and 3 unique molecular probes. The number of positive beacons, their detection timing (indicated by rise of fluorescent signal above a predetermined baseline cycle threshold) and the results of sample processing controls, allow the test to distinguish among the following results: no TB; TB detected, rifampicin resistance detected; TB detected, no rifampicin resistance detected; TB detected, rifampicin resistance indeterminate; and an invalid result.

Revised National TB Control Programme (RNTCP) is also currently using Xpert MTB/RIF to diagnose pulmonary TB, paediatric TB, extrapulmonary TB and rifampicin resistance and Multi Drug Resistance Tuberculosis in high risk populations like HIV positive as recommended by WHO under 2013 policy recommendations.

**MATERIALS AND METHODS**

This study is done at IRL MRTB Hospital M.P., India. The sputum samples are received from Indore M.P. The study period is from 2015 to August 2016. A total of 4595 patients with symptoms suggestive of pulmonary tuberculosis including both new cases and on treatment. All specimens were collected in pre-sterilized falcon tubes with three layer packing system, after through rinsing of the oral cavity with clean water. Samples along with prescribed Performa containing details of patients like Name, Address, Age, Sex, HIV status, and Name of the referring centre was received in the Microbiology Laboratory.

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<th>Table/Fig-1: Total HIV TB positive cases &amp; Rif Sensitive cases</th>
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<tr>
<td>Out of these 1087 patients which were reported MTB positive 127(11.6%) were reported positive for (HIV +TUBERCULOSIS). Of these 127 Co-infected cases 118 (92.9%) cases were sensitive to rifampicin (RIF) and...</td>
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9 (15.78%) cases were showing resistance to rifampicin (Rif) Drug as shown in Table/Fig-2:

![Table/Fig-2: TB-HIV Co-infected, cases sensitive to rifampicin (Rif) and cases showing resistance to rifampicin (Rif)](image)

DISCUSSION

Globally, 51% of notified TB patients had a documented HIV test result in 2014.[12] India accounts for about 10% of the global burden of HIV-associated TB. The mortality in this group is very high and every year: 42000 people die every year among TB/HIV co-infected patients.[12]

In given study 11% patients were found to be HIV–TB co-infected. As per the WHO Global Report on Tuberculosis 2013, India accounts for 64,000 MDR TB cases out of 300,000 cases estimated globally to occur among the notified pulmonary TB cases annually. [12] High prevalence of MDR-TB was detected among HIV positive cases (15.78%) which in accordance with the study done by Sethi et al., at PGIMER, Chandigarh for a span of 41 months who reported significantly higher association of MDR-TB (27.3%) with HIV seropositive patients as compared to HIV seronegative patients (15.4%).[13]

Cartridge Based Nucleic Acid Amplification testing (CB-NAAT) is a new operational system recommended by WHO. Results from 12 single centre evaluation studies with varying design and study population and reviewed by WHO reported the sensitivity in detecting TB from 70%-100% in culture positive patients and around 60% in those with smear negative disease and specificity ranging from 91%-100% and average rifampicin sensitivity and specificity around 98% and 99%. [8]

Studies from different part of world have reported high sensitivity and specificity by using Xpert MTB/RIF test based on this assay. In a study by Raizada et al., that covered a population of 8.8 million across 18 sub-district level tuberculosis units (TU) in India, Overall 28% TB cases were bacteriologically confirmed, of which 27.6% TB cases were detected on Xpert MTB/RIF against smear positivity rate of 12.9%. However, of 9 Xpert MTB/RIF negative and culture positive cases, 8 were detected on smear microscopy too. Positive predictive value (PPV) for rifampicin resistance detection by Xpert MTB/RIF was 97.7%.[14] Similar study on HIV positive adults referred to DOTS centre with pulmonary symptoms suggestive of tuberculosis Singh and co-authors concluded that “CBNAAT is easily done, valid, more accurate and reliable alternative to sputum microscopy for detection of pulmonary tuberculosis in HIV patients”. [15]

CONCLUSION

In the rapidly evolving era of TB and HIV co-infection, updated knowledge as well as changing research priorities, particularly with respect to new TB diagnostics is the need of the hour. The Gene Xpert system can be used as the initial diagnostic test in individuals suspected of having MDR-TB or HIV associated TB as it can test 4 modules with capacity to perform 15 to 20 tests in one working day and the result is available in less than 2 h and hence screening capacity of healthcare centre can be increased. Use of Xpert has significantly increased TB finding and it has also significantly increased MDR case finding and cost wise it is much less than performing culture and DST. The system can be operated under diverse environmental conditions, with minimally trained staff and least biosafety concerns.

Authors’ contributions statement: AK designed and supervised the study, provided research laboratory. VA scientifically advised the study. VC, reviewed the literature, JK prepared, preliminarily drafted the manuscript & edited the final version of the manuscript. ND, AV, DP & NAA practically carried out the study. All authors reviewed and approved the final version of the manuscript.

REFERENCES