IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 11 Ver. 1 (November. 2018), PP 50-52
www.iosrjournals.org

Roleof Cartridge-Based Nucleic Acid Amplification Test (Cbnaat) For Early Diagnosis of Tuberculosis: A Retrospective Study

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Abstract:
Background: *About one fifth of global Tuberculosis (TB) burden present in INDIA and it is ninth leading cause of death worldwide. It is very important to early diagnose and treat Tuberculosis cases to stop transmission. Smear microscopy is the cornerstone but sensitivity and its inability to detect drug resistance limits its role in TB controland it has only modest sensitivity and poor positive predictive value. Culture is the gold standard but its results typically not available for 2-6 weeks. We compared the cartridge-based nucleic acid amplification test (CBNAAT) results for diagnosis of pulmonary and extra pulmonary tuberculosis with the conventional methods like sputum smear and culture examination.*
Material and Methods: *We conducted a retrospective study in department of pulmonary medicine, BURDWAN MEDICAL COLLEGE BURDWAN, WEST BENGAL, and RAJENDRA INSTITUTE OF MEDICAL SCIENCES, RANCHI, JHARKHAND, INDIA to analyse the result of CBNAAT in diagnosis of tuberculosis from Jan2017-Dec 2017. Data was collected from DOTS centre and CBNAAT centre. A total no of 200 cases were studied.*
Results: *Total 200 samples for CBNAAT taken for this study. Mean age of the study population was 30.3±9.24 years. Of these 200 samples, 173 were sputum/BAL samples and 27 were extra pulmonary samples. We found rifampicin resistance rate of 4.6% (8/173) in pulmonary tuberculosis cases, no rifampicin resistance detected in extra pulmonary samples. CBNAAT could identify 43 cases (24.8%) that were smear negative. We found TB-HIV coinfection rate of 3.33%. 38(21.96%) Sputum/BAL samples were AFB smear positive and 135(78.03%) % were negative. Chi square test was applied; P value is <0.001. For pulmonary samples, the sensitivity and specificity for CBNAAT samples were 80.2% and 90.6% respectively; while that for sputum smear were 42.6% and 98.1% respectively. For extrapulmonary samples, the sensitivity and specificity for CBNAAT samples were 84.9% and 94.2% respectively; while that for sputum smear were 61.3% and 100% respectively.*
Conclusions: *We found CBNAAT is an important diagnostic modality especially in sputum negative patients for early diagnosis and treatment in lesser time as compared to conventional sputum microscopy. It also detects the rifampicin resistance with high specificity to start early treatment.*
Keywords: *CBNAAT, M. tuberculosis, Smear negative AFB, MDR TB, microscopy*

Date of Submission: 20-10-2018 Date of acceptance: 03-11-2018

I. Introduction

India has the highest number of Tuberculosis (TB) cases in the world, with over two million TB cases every year. According to WHO global TB report, the estimated incidence of TB is 2.2 million and prevalence is 2.5 million with mortality of 0.22 million.There were 580,000 estimated new cases of MDRTB (Multi-drug resistant TB) and Rifampicin resistant TB (RRTB); among them 125,000 (20%) were reported. Early and accurate diagnosis is the main step in controlling TB. Culture methods and drug susceptibility testing is complex and takes longer time around 6-8 weekswhichresults in inappropriate or in effective treatment and in increased morbidity. To overcome this issue there was a need for a simple and rapid diagnostic tool at least for high-burden countries .A new diagnostic test cartridge based nucleic acid amplification test (CBNAAT) was developed which was rapid, fully automated and was based on polymerase chain reaction (PCR) that detects deoxyribonucleic acid (DNA) directly from the clinicalspecimen and also detects rifampicin resistance and delivered the results in about 120 minutes.In this study, we compared the CBNAAT results fordiagnosis of pulmonary and extrapulmonary tuberculosis withthe conventional methods like sputum smear and solid cultureexamination.

WHO recommended use of a Cartridge Based Nucleic Acid Amplification test (CB-NAAT), for diagnosis of TB in December 2010.It is a cartridge based nucleic acid amplification test (CBNAAT) that does

not have any specific pre-requites for its set-up and does not require much technical training. Also the reagent used for processing is bactericidal and tubercle bacilli are inactivated in vitro, biosafety risks are eliminated, thus enabling its use as a rapid point-of-care diagnostic test.

II. Method

We conducted a retrospective study in the department of pulmonary medicine, BURDWAN MEDICAL COLLEGE BURDWAN, WEST BENGAL, INDIA and RAJENDRA INSTITUTE OF MEDICAL SCIENCES, RANCHI, JHARKHAND, INDIAto evaluate the use of CBNAAT from January 2017 to December 2017. Data was collected from ART centre, DOTS centre and CBNAAT centre. We collected total number of tested for CBNAAT, HIV status, result of smear microscopy for AFB and CBNAAT. Specimen subjected to CBNAAT was either sputum, gastric lavage, BAL or extrapulmonary fluid sample (lymph node,pus, Pleural fluid, pericardial fluid, synovial fluid, ascitic fluid, cerebrospinal fluid). The smearpositive specimens were evaluated within two weeks at the latest, while the smear-negative specimens were studied immediately after the growth of culture. All the specimens which were culture positive and mycobacterium tuberculosis, resistance to rifampicin (MTB/RIF) assay negative and specimens that were culture negativeand MTB/RIF assay positive were retested twice. The lastresult was included for the analysis.

III. Results

Of these 200CBNAAT samples, 173were sputum/BAL samples and 27 were extra pulmonary samples. We found rifampicin resistance rate of 4.6% (8/173) in pulmonary tuberculosis cases, of which 2 were HIV positive. Mycobacterium Tuberculosis was detected in 59.25% of extrapulmonary samples subjected to CBNAAT. There was no rifampicin resistance detected in extra pulmonary samples. CBNAAT could identify 43cases (24.8%) that were smear negative (Table 1). We found TB and HIV co-infection rate of 3.33%. Mean age of the population was 30.3±9.24years. Two cases of MDR TB were detected and both were pulmonary Koch's. Only 1 patient had recurrent TB while rest was new cases. Amongthe samples provided 144 (72%) were males and 56 (28%) female.The comparison of CBNAAT, sputumsmear against solid culture is shown in Table 1.

Sample type		Pulmonary(n-173)	Extra-pulmonary(n-27)
Test type	Result		
Sputum smear	Negative	135(78.03%)	21(77.77%)
	Positive	38(21.96%)	6(22.22%)
CBNAAT	Negative	72(41.61%)	16(59.25%)
	Positive	101(58.38%)	11(40.74%)

IV. Discussion

India contributes to one fifth of global TB cases worldwide. Early diagnosis and treatment is critical to stop transmission. CBNAAT is one diagnostic modality that has been approved by WHO in the diagnosis of TB. CBNAAT has higher sensitivityfor detection of pulmonary and extrapulmonary tuberculosiscases.We found in our study CBNAAT detected around 24.8% of patients who were smear negative. The rate of rifampicin resistant TB detected by CBNAAT was 4.6% and among HIV patients it was 3.33%.

In the present study, only 200 specimens were included; among them 173 were pulmonary and 27 were extrapulmonary. The sensitivity of CBNAAT for pulmonary samples was 79% when compared to sputum smear which was 42%. The sensitivity of CBNAAT for extrapulmonary samples was 86% when compared to sputum smear which was 61%. The sensitivity of CBNAAT in smear-positive, culture-positive and smear-negative, culture-positive pulmonary samples was 100% and 66.67% respectively. Sensitivity of smear negative pulmonary samples can be increased by including more than one sample for diagnosis.

In a study done by Armand et althe sensitivity of CBNAAT in 60 pulmonary samples which included sputum, BAL, bronchial aspirate and gastric aspirate was 79%. Among individual extrapulmonary samples, the sensitivity of CBNAAT was highest among lymph nodes (94.74%) when compared to sputum smear (73.68%). Inclusion of CBNAAT in the initial diagnosis of tubercular lymphadenopathy in addition to the FNAC would decrease the over diagnosis of tuberculosis and injudicious use of anti-tuberculosis treatment (ATT).

Another study done by Dewan et al., done in Delhi found rifampicin resistance of 10%. This high resistance to rifampicin compared to our study may be due to higher prevalence of MDR TB in north India and also referral from multiple states.

The prevalence of MDR TB is 2-3% among new cases and 12-17% among retreatment cases. A study done by Sharma et al found prevalence of MDR TB to be 1.1% in new cases and 20% in retreatment cases.13 Another multi-centric study done by Sukhdev et al., found prevalence of MDR TB to be 2-3% in new cases and 12-17% among retreatment cases.

To conclude, CBNAAT is one of the rapid diagnostic tests available in the country and it should be routinely used under the public and private health sectors efficiently to detect a tuberculosis case.

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Manish Kumar Munda. "Roleof Cartridge-Based Nucleic Acid Amplification Test (Cbnaat) For Early Diagnosis Of Tuberculosis: A Retrospective Study" IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 11, 2018, pp 50-52.