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Pulmonary Medicine

CBNAAT IN DIAGNOSIS OF PULMONARY AND EXTRA PULMONARY TUBERCULOSIS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

INTRODUCTION: Tuberculosis is the ninth leading cause of death worldwide. Tuberculosis incidence in India is 2.74 million including 0.13 million drug resistant cases. According to WHO 0.41 million deaths in India are due to tuberculosis in 2017. Sputum smear microscopy is facing variable sensitivity issue particularly in sputum smear-negative, extrapulmonary disease and drug-resistant Tuberculosis. Conventional solid culture techniques take long turnaround time of 2-6 weeks and is costly. To overcome this problem, WHO current policies and guidance recommend to use Xpert MTB/RIF as an initial diagnostic test.

AIM: To study the utility of CBNAAT in diagnosis of Pulmonary and Extrapulmonary tuberculosis .

RESULTS: Among 313 samples, 149 were pulmonary and 164 were extra pulmonary. Among 149 pulmonary samples, 70 (46.97%) were sputum smear positive whereas MTB was detected in 109 (73%) samples through CBNAAT. Out of 109 samples, 106 samples were found to be rifampicin sensitive and 3 (4.2%) were rifampicin resistant. 40 (26.8%) samples that were negative for CBNAAT subjected to bronchoscopy, MTB was detected in 10 cases (25%) in BAL CBNAAT which were rifampicin sensitive . Extra pulmonary samples 164 yielded 16 (9.8%) positive result for MTB and 0% rifampicin resistance.

CONCLUSION: CBNAAT is a simple, rapid and a better diagnostic test for detection of pulmonary and extra pulmonary tuberculosis. Enhanced diagnostic yield for smear negative pulmonary and extra pulmonary tuberculosis is well documented.

KEYWORDS : Cartridge-based Nucleic Acid Amplification Test (cbnaat); Tuberculosis; Sputum Smear.

INTRODUCTION:

Tuberculosis is the ninth leading cause of death worldwide. India contributes to about one fifth of global TB burden. According to Global Tuberculosis Report 2018, Tuberculosis incidence in India is 2.74 million including 0.13 million drug resistant cases. According to WHO 0.41 million Deaths in India are due to tuberculosis in 2017.[1]

Most easily available diagnostic method i.e. Sputum smear microscopy only 49% of cases can be detected in India. Culture on Lowenstein Jensen (LJ) medium, "the gold standard test", takes 2- 8 weeks and it is costly.[3] New generation liquid culture diagnostics and molecular line probe assays are costly and needed biosafety measures and specialised staff.

To overcome this problem, WHO current policies and guidance recommend that Xpert MTB/RIF be used as an initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB[2].

CBNAAT which was rapid, fully automated and was based on polymerase chain reaction (PCR) that detects deoxyribonucleic acid (DNA) directly from the clinical specimens and also detects rifampicin resistance[4]. This diagnostic test was designed to purify, concentrate, amplify and identify targeted rpoB nucleic acid sequences, and delivers the results in about 120 minutes. [5,6,7]

Early detection of TB cases is the key to successful treatment and reduction of disease transmission and most deaths from TB could be prevented with early diagnosis and appropriate treatment.

In this study, we compared the CBNAAT results for diagnosis of pulmonary and extrapulmonary tuberculosis with the conventional methods like sputum smear examination.

MATERIAL & METHODS:

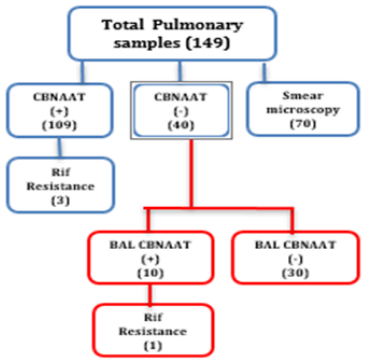
We conducted a retrospective study in Dr.Pinnamneni Siddartha Institute of Medical Sciences (Dr.PSIMS & RF), Gannavaram, A.P ,India. Study was done in Department of Pulmonary Medicine to analyze the utility of CBNAAT from July 2017-July 2018. We included all patients who were subjected to CBNAAT in the study period. To diagnose tuberculosis the investigations included sputum smear microscopy by light emitting diode (LED) fluorescent microscopy (FM) and CBNAAT depending upon the type of specimen. Non-sterile clinical specimens were processed by conventional N-acetyl-l-cysteine–NaOH method. After decontamination, Place the fixed smear on a staining rack and flood slide with rhodamine-auramine for 15 minutes. Wash off the stain with distilled water. Flood slide with fluorescent decolourizer (i.e. acid-alcohol) for 2-3 minutes. Rinse with distilled water. Flood slide with potassium permanganate for 3-4 minutes. Rinse with distilled water and air dry. Examined slides can be screened on high power (400X) and verified under oil immersion. Smears can be examined in a fraction (about 25% less) of the time with increased sensitivity (10% higher) when compared with ZN microscopy methods.

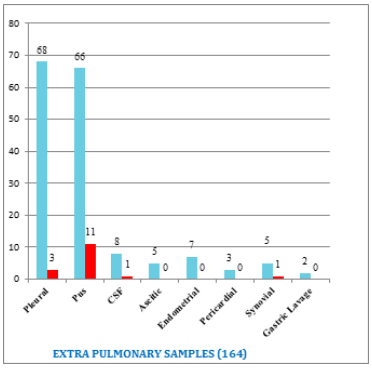
For CBNAAT examination the Specimen was collected in Falcon tubes and analysis was done on the same day and results were given within a day. TB detection was done by Xpert MTB/ RiF assay, made by Cepheid (Sunnyvale, CA, United States). All specimens were processed according to the GeneXpert system operator manual given by Central TB division, Government of India. The sample reagent was added at a 3:1 ratio to clinical specimens. The closed specimen container was manually agitated twice during a 15-minute period at room temperature, before 2 ml of the inactivated material was transferred to the test cartridge. 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. Xpert MTB/RIF cartridge is a disposable, single self-enclosed test unit in which all steps of NAAT i.e. Sample processing, PCR amplification and detection are automated and integrated.

RESULTS:

Among 313 samples, 149 were pulmonary and 164 were extra pulmonary. Among 149 pulmonary samples, 70 (46.97%) were sputum smear positive whereas MTB was detected in 109 (73%) samples through CBNAAT. Out of 109 samples, 106 samples were found to be rifampicin sensitive and 3 (4.2%) were rifampicin resistant. 40 (26.8%) samples that were negative for CBNAAT subjected to bronchoscopy, MTB was detected in 10 cases (25%) in BAL CBNAAT which were rifampicin sensitive The proportion of extra pulmonary samples received from different anatomical sites were: pleural fluid 68, Pus 66, CSF 8, Ascitic 5, Endometrial 7, Pericardial 3, Synovial 5, Gastric lavage 2 of which CBNAAT positive from pleural fluid were 3 (4%), Pus 11 (16%), CSF 1 (12%) and Synovial fluid 1 (2%). Total CBNAAT extrapulmonary yield is 16

(9.8%) and 0% rifampicin resistance.





DISCUSSION:

Our study findings suggest that CBNAAT has higher sensitivity for detection of pulmonary and extrapulmonary tuberculosis cases. The WHO 2012 has also recommended the CBNAAT for routine use under programmatic conditions.[3]

In present study, among 313 samples, 149 were pulmonary and 164 were extra pulmonary. Among 149 pulmonary samples, 70 (46.97%) were sputum smear positive whereas Mtb was detected in 109 (73%) samples through CBNAAT. Out of 109 samples, 106 samples were found to be rifampicin sensitive and 3 (4.2%) were rifampicin resistant. 40 (26.8%) samples that were negative for CBNAAT subjected to bronchoscopy, MTB was detected in 10 cases (25%) in BAL CBNAAT which were rifampicin sensitive In a study done by Amiya Kumar Dwari et al., reported 34% yield for sputum CBNAAT, 10.7% for BAL-CBNAAT and together it was 44.7%.[8]

Avashia S et al., reported 47.2% gain sputum CBNAAT positivity among smear negative TB cases[9]

In a study done by Virupakshappa V et al., conducted on 267 sputum/BAL samples and 23 extra pulmonary samples. They found rifampicin resistance rate of 2.4% in pulmonary tuberculosis cases[10].

	Sputum Cbnaat Positive	Bal Cbnaat Positive	Rifampicin Resistance
Present Study	73%	25%	4.2%
Amiya Dwari Et Al.	34%	10.7%	-
Avashia S Et Al.	47.2%	-	-
Virupaksha V Et Al.	-	-	2.4%

In our study Extra pulmonary samples 164 yielded 16 (9.8%) positive result and 0% rifampicin resistance

In a study done by Saurabh Jain & Ramesh Agrawal, out of 1736 samples, 1537 were pulmonary & 199 Extrapulmonary. Samples positivity rate were (727) 41.87 %, of which (680) 39.17% are Rifampicin sensitive & (47) 2.7% are resistant for Mycobacterium tuberculosis. The most common extrapulmonary samples are pleural fluid 43.7%, pus 27% & cervical lymph nodes 16.6% . 37 extrapulmonary samples were positive for Mycobacterium tuberculosis. Out of this, 33 are sensitive & 4 were resistant to Rifampicin.[13]

Irfan ullah et al., conducted a study on rapid detection of MTB in 168 extra pulmonary tuberculosis samples using CBNAAT. MTB was detected 60 (35.7%) samples[11].

Gour Sanjay M et al., done a Retrospective analysis of 267 suspected extra pulmonary tuberculosis smear negative samples. MTB was detected in 47(17.6%) samples. Of these 47 samples, 44 (93.6%) were sensitive to rifampicin and 3(6.38%) were resistant to rifampicin[12].
Our study findings suggest that CBNAAT has higher sensitivity for detection of pulmonary and extrapulmonary tuberculosis cases.

CONCLUSION:

CBNAAT is a simple, rapid and a better diagnostic test for detection of pulmonary and extra pulmonary tuberculosis. Enhanced diagnostic yield for smear negative pulmonary and extra pulmonary tuberculosis is well documented. As it can be used close to the point of care by operators with minimal technical expertise, enabling early diagnosis of TB and simultaneous assessment of rifampicin resistance within a short time, establishing more centres will not only improve the outcomes but also reduces the economic burden.

REFERENCES:

1. WHO | Global tuberculosis report 2017. Available from URL: http://www.who.int/tb /publications/global_report/en/.
2. Weyer K, Mirzayev F, Migliori GB, Van Gemert W, D'Ambrosio L, Zignol M, et al. Rapid molecular TB diagnosis: evidence, policy making and global implementation of Xpert MTB/RIF. Eur Respir J. 2013;42(1):252–71.
3. Xpert MTB/RIF implementation manual IMPLEMENTATION MANUAL. 2014. Website: www.who.int/tb.
4. Chaudhuri AD. Recent changes in technical and operational guidelines for tuberculosis control programme in India-2016: A paradigm shift in tuberculosis control. J Assoc Chest Physicians. 2017;5:1-9.
5. Greco S, Girardi E, Navarra A, Saltini C. Current evidence on diagnostic accuracy of commercially based nucleic acid amplification tests for the diagnosis of pulmonary tuberculosis. Thorax. 2006; 61:783-90.
6. Centres for Disease Control and Prevention (CDC). Updated guidelines for the use of nucleic acid amplification tests in the diagnosis of tuberculosis. MMWR Morb Mortal Wkly Rep. 2009; 58:7-10.
7. Ioannidis P, Papaventsis D, Karabela S, Nikolaou S, Panagi M, Raftopoulou E, et al. Cepheid GeneXpert MTB/RIF assay for mycobacterium tuberculosis detection and rifampicin resistance identification in patients with substantial clinical indications of tuberculosis and smear-negative microscopy results. Journal of Clinical Microbiology. 2011;49(8):3068-70.
8. Dwari, A.K.,Jha, S.Haldar, D.Biswas, B.Saha, S.K.,Roy, P.P., Mandal,A.Maji,B.(2018). CBNAAT Co-Testing of Sputum and BAL Fluid with Sputum Microscopy: May it Halt the March of Tuberculosis! 12(6), LC22-LC24.
9. Avashia S, Bansal D, Ahuja K, Agrawal V. Comparison of conventional methods with gene xpert mtb/rif assay for rapid detection of mycobacterium tuberculosis and rifampicin resistance in extra-pulmonary samples. Int J Med Res Rev 2016;4(2):181-185. doi: 10.17511/ijmrr.2016.i02.010.
10. Virupakshappa V ,Ranganath M ,Manjunath MP ,Mahendra M ,et al .utility of CBNAAT in diagnosis of mycobacterium tuberculosis in a teritary care teaching hospital in south india .IP indian journal of immunology and respiratory medicine ,jan-march ,2018:3(1):3-6 .
11. Ullah ,javaid ,masud h ,ali m ,basit a ,ahmad w ,younis f et al.rapid detection of mycobacterium tuberculosis and rifampicin resistence in extrapulmonary tuberculosis and sputum smear negative pulmonary suspects using xpert MTB/RIF.J Med microbiology 2017 april ,66 (4):412-418.
12. Gour Sanjay M et al., done a Retrospective analysis of 267 suspected extra pulmonary tuberculosis smear negative samples. MTB was detected in 47(17.6%) samples. Of these 47 samples, 44 (93.6%) were sensitive to rifampicin and 3(6.38%) were resistant to rifampicin.
13. Jain S, Agrawal R. Rapid Diagnosis of Pulmonary and Extrapulmonary Tuberculosis by Cartridge-Based Nucleic Acid Amplification Test (CBNAAT). Int J Med Microbiol Trop Dis 2019;5(4):204-206.