



Role of Cartridge based nucleic acid amplification test (CBNAAT) in new sputum negative pulmonary tuberculosis

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Abstract:

Introduction: Diagnosis of pulmonary tuberculosis in sputum negative patients for acid fast bacilli is challenging till today. It is a fact that 50-60% patients of pulmonary tuberculosis are sputum negative microscopically. Smear microscopy is the easiest, commonest and widely employed tool for confirmatory diagnosis of pulmonary tuberculosis, but it has low sensitivity and specificity. Sputum culture for *Mycobacterium tuberculosis* bacteria can increase the diagnostic yield by 20-40%, but it takes long duration of 2-8 weeks when solid media are used or 10-14 days when radiometric system in liquid media are used. Delayed diagnosis causes increased rate of disease transmission in the community. The role of newly introduced cartridge based nucleic acid amplification test (CBNAAT) in the revised national TB control program (RNTCP) is highly promising with a higher yield of bacteriological diagnosis in sputum negative pulmonary tuberculosis patients with detection of rifampicin resistance within 2 hours only. **Aims and objectives:** The current study is to find out efficacy of CBNAAT in diagnosis of new sputum negative pulmonary tuberculosis patients. The detection of rifampicin resistance is also done in those patients. **Materials and Methods:** Sputum samples of 100 sputum negative pulmonary tuberculosis patients were sent to District CBNAAT center in sterilized falcon tube container. The CBNAAT result were analyzed. **Results:** *Mycobacterium tuberculosis* was detected in thirty one patients (31%). Not a single case was detected as resistant to rifampicin. **Conclusion:** CBNAAT helps in increased case detection rate in lesser time in new sputum negative pulmonary tuberculosis patients. Rifampicin resistance was not detected in any patient.

Key words: CBNAAT, pulmonary tuberculosis, *Mycobacterium tuberculosis*, RNTCP

Introduction:

Tuberculosis is an age old disease. In 1882, Sir Robert Koch discovered *Mycobacterium tuberculosis* (MTB) as the causative agent for this disease. According to the Global Tuberculosis report 2014 of World Health Organization (WHO), tuberculosis (TB) remains one of the most dangerous communicable diseases. The disease usually affects the lungs known as pulmonary tuberculosis (PTB) and spreads by droplet aerosol transmission from infected patient to healthy person. Early diagnosis is imperative for early patient management and successful patient outcomes in order to prevent the further spread of this disease. But even today, the diagnosis of TB remains elusive. The symptoms of pulmonary TB (PTB) like cough, fever, hemoptysis, weight loss are non-specific, and these may occur in any

chronic lung infection. Chest X-Ray is also highly diversified for diagnosis of pulmonary TB. Till today, no biochemical or serological test is valid and acceptable for diagnosis of pulmonary TB. In this scenario, the microscopic demonstration of *Mycobacterium tuberculosis* bacilli in sputum samples is the only method for confirmatory diagnosis of PTB. Sputum microscopy is accepted worldwide as the first line test and it is a rapid method (few minutes), as well as cost effective (free under RNTCP). However, it is less sensitive and only 50 to 60% of new cases of PTB can be diagnosed.^{1,2} Sputum culture has a higher diagnostic yield, but it is an expensive, more time consuming, (2 to 4 weeks), non-easy availability test that is done at few reference laboratories.³ Smear negative pulmonary TB (SNPT) constitutes nearly half of the PTB patients. Ten to twenty percent of TB transmission in the community are attributable to SNPT

patients.⁴ So, early diagnosis and treatment of SNPT patients is essential to reduce the global burden of TB. The WHO policy guidance on the use of CBNAAT was issued in December 2010. The recommendations were that it should be used as the initial diagnostic test in individuals at risk of having MDR-TB or HIV-associated TB (strong recommendation). In 2013, the use of CBNAAT recommendation was extended as Xpert MTB/RIF may be used rather than conventional microscopy and culture as the initial diagnostic test in all adults suspected of having TB (conditional recommendation) acknowledging resource implications, high-quality evidence.⁵ In our institution falling under Bareilly District Tuberculosis center, this test was implicated in January 2017 for detection of *Mycobacterium tuberculosis* in new smear negative pulmonary TB patients. So, an institutional based study was imperative to know about the efficacy of CBNAAT in diagnosis of PTB in such patients.

Materials and Methods:

This study was conducted by taking randomized samples of 100 sputum negative new pulmonary TB patients attending at Rohilkhand Medical College, Bareilly (both out patients and inpatients) in the department of pulmonary medicine from a period from January 2017 to December 2017. A provisional diagnosis of PTB was made as per WHO criteria (cough for 2 weeks or more, unexplained fever for 2 weeks or more, loss of appetite and body weight, abnormal chest x-ray). All of them were subjected to two samples of sputum smear microscopic examination at designated microscopic center of this institute as per norms of Revised National Tuberculosis Control program (RNTCP) and chest X-ray. Patients with smear negative, with or without X-ray signs of PTB were then subjected to CBNAAT test by sending sputum samples in falcon tubes

to the district CBNAAT center; within 3 days of sputum microscopy, report was revealed as negative. The CBNAAT result was obtained in proper format as TB detected, no TB detected, sensitive or resistant to Rifampicin. The following were the inclusion and exclusion criteria for this study-

Inclusion criteria: -

- Age- equal or more than 18 years, both sexes, new PTB suspects
- Initial two sputum smear samples are negative for acid fast bacilli under fluorescent microscopy.

Exclusion criteria:-

- Patients with past history of tuberculosis or treated with a course of anti-tubercular drug therapy
- Patients with co-morbidities of cardiovascular and renal diseases
- Associated HIV infection (positive)

Ethics:- The Institutional Ethics Committee (IEC) of Rohilkhand Medical College, Bareilly had approved the conduct of this study.

Results:

In this study, 34 patients were female and 66 patients were male. Age distribution is as summarized in **Table I**. Radiological abnormality in chest X-ray and CBNAAT result is summarized in **Table II** and **III**. Types of chest radiological abnormality was correlated with CBNAAT in **Table IV**.

Table I: Age distribution of patients

Age group (years)	Number (n)	Percentage (n %)
18-30	26	26
31-45	39	39
46-60	19	19
61 and above	16	16
Total	100	100

Table II: Chest X-ray abnormality suspicious of PTB

Chest X-ray	Number (n)
Infiltration	79
Infiltration and cavitation	21
Total (n)	100

The result of this study shows that maximum incidence of smear negative PTB is found between age group of 18 to 45 years (65%). Chest X-ray abnormality is present in all patients and is the main investigatory tool for diagnosis of smear negative pulmonary tuberculosis among the PTB suspects. Infiltration in chest X-

Conclusions:

India continues to have the highest number of tuberculosis cases in the world. Global TB report 2017 released by World Health Organization (W.H.O.) estimated 10.4 million new TB cases worldwide.⁶ Seven countries accounted for most of the total burden with India having the maximum burden followed by Indonesia, China, Pakistan, Nigeria and South Africa (W.H.O. 2016 report released in 2017). Pulmonary TB constitutes maximum of all tuberculosis among which nearly about half are smear negative and those cases pose a challenge for bacteriological diagnosis. Chest radiology with a clinical background is the main tool for diagnosis of sputum negative tuberculosis.

Table III: CBNAAT result

CBNAAT	Numbers (n)	Rifampicin resistant	Numbers
Detected	31	Detected	0
Not detected	69	-	
Total (n)	100		0

Table IV: CBNAAT and Chest X-ray correlation

X-ray lesion	Number of patients	Numbers of CBNAAT detected	%
Infiltration	79	17	21.51
Infiltration and cavity	21	14	66.61
Total	100	31	31

Statistical analysis: - All results were analyzed by applying Chi-square test. P value was <0.001 and all the results are highly significant

-ray is the most common radiological abnormality (79%) and next to it is a combination of both infiltration and cavitation (21%) in sputum negative PTB patients. A significant percent (31%) of smear negative patients were diagnosed by CBNAAT. Efficacy of CBNAAT in detecting tuberculosis is more in infiltrative and cavitary lesion (66.6%) rather than infiltrative lesion alone (21.5%) New SNPT patients hardly show any resistance to Rifampicin if at all Mycobacteria is detected by CBNAAT.

Sputum culture in SNPT patients can provides rapid diagnosis which is a time consuming process and can be done in a few available reference laboratories only. Newly introduced rapid method of CBNAAT by W.H.O. is very helpful and a promising tool for early diagnosis and treatment of smear negative pulmonary tuberculosis patients with its role in detection of Mycobacteria and rifampicin resistance within 2 hours only and that will definitely result in decreased TB transmission and global burden of

tuberculosis. Higher chance of mycobacterial detection by CBNAAT is among patients with a combined chest-radiological abnormality of infiltration and cavitation^{7,8,9}. CBNAAT can also help in diagnosis of initial multi-drug resistant pulmonary tuberculosis.

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