(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume4, Issue 1, Page No: 17-22
January-February 2021

Assessment of Diagnostic Utility of Cartridge Based Nucleic Acid Amplification Test in Bronchoalveolar Lavage of Sputum Smear Negative Pulmonary Tuberculosis Patients

Kumar Adesh[1](MD), Gupta Kumar Ashish[2](MD), Gautam Kumar Aditya[3](M.D), Yadav Prashant [4] (MD), Kumar Ajeet[5] (MD)

[1]Professor, [2]Associate Professor, [3.4]Assistant Professor, [5]Junior Resident

Department of Respiratory Medicine, UP University of Medical Sciences, Saifai, Etawah ,UP

***Corresponding Author:**
Dr Prashant Yadav

Assistant Professor, Department Of Respiratory Medicine, UP University of Medical Sciences , Saifai, Etawah, UP. 206130

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

ABSTRACT

***Background* & Objective**

Sputum smear negative pulmonary tuberculosis (SSN-PTB) is a common clinical problem faced by the clinicians as approximately 50% of pulmonary tuberculosis cases. In India, a high TB burden country there is scarcity of literature regarding Mycobacterium Tuberculosis / Rifampcin assay in Bronchoalveolar lavage fluid for diagnosis of pulmonary tuberculosis. Therefore this study was planned to assess diagnostic utility of Cartirage based nucleic acid amplification test in Brochoalveolar lavage fluid for early diagnosis of pulmonary tuberculosis in sputum smear negative pulmonary tuberculosis cases.

Materials and Methods

A hospital based cross sectional study was done from February 2017 to February 2020 in 147 sputum smear negative pulmonary tuberculosis patients who were fulfilled the inclusion criteria were subjected to flexible fibreoptic bronchoscopy and data were collected from patients according to a predesigned proforma.

Results

The mean age of the patients in this study was 43.7 $\pm$ 16.8 years with a range from 18 to 70 years. There were 82 (55.78%) males and 65 (44.22%) were females. In this study CBNAAT was found positive in 70 (47.61%) patients and out of 70 , Rifampicin resistance was detected in 09 (12.86%) patients. MGIT was found positive in 58 (39.45%) patients .The Sensitivity, Specificity, Positive Predictive Value and Negative predictive value of CBNAAT in BAL fluid of sputum smear negative pulmonary tuberculosis patients were 86.20%, 73.68%, 71.42% and 87.50% respectively.

Conclusion

CBNAAT in BAL can be used to confirm the early diagnosis of pulmonary tuberculosis in sputum smear negative pulmonary tuberculosis cases and due to rapidity and ability to detect rifampicin resistsance simultaneously, it will be further useful to dealt with such cases of drug resistance without undue delay .

Keywords: CBNAAT, MGIT , BAL , Sputum Smear Negative Pulmonary Tuberculosis.

INTRODUCTION

Tuberculosis (TB) is a leading global public health problem, with an extremely high mortality if left untreated.Detecting patients with active pulmonary tuberculosis (PTB) disease an important component of tuberculosis (TB) control as early diagnosis and appropriate treatment renders these patients non-

infectious and interrupts the chain of transmission of TB and also prevent sequalae of pulmonary tuberculosis[1]. In Revised National Tuberculosis Control Programme (RNTCP) of Government of India, the diagnosis of pulmonary tuberculosis is based on sputum smear examination [2]. In many patients with a compatible clinical and radiological picture, sputum smears do not reveal acid-fast bacilli (AFB).Sputum smear negative pulmonary tuberculosis (SSN-PTB) is a common clinical problem faced by the clinicians as approximately 50% of pulmonary tuberculosis cases are sputum smear negative for AFB [3].

Currently diagnostic criteria for SSN-PTB include at least two sputum smear negative for AFB, radiographic abnormalities consistent with active PTB, no response to a course of broad spectrum antibiotics (except in a patient for whom there is a laboratory confirmation or strong clinical evidence of HIV infection), and a decision by a clinician to treat with full course of anti TB chemotherapy [4]. A number of studies confirm the usefulness of fiberoptic bronchoscopy (FOB) in the diagnosis of PTB [5,6]. The main advantage of FOB is its ability to visualize the bronchial tree and collect samples directly from the site of pathology. FOB with bronchial aspiration and broncho-alveolar lavage (BAL) under local anesthesia is a relatively safe procedure and well tolerated by the patients [7-9].

Cartridge based nucleic acid amplification (CB-NAAT) assay first fully automated test for mycobaterial tuberculosis detection with rifampcin resistance. It gives results within 2 hours and diagnostic accuracy for pulmonary TB has been reported high [10,11].

The use of CBNAAT recommendation was extended and may be used rather than conventional microscopy and culture as the initial diagnostic test in all adults suspected of having TB in 2013, [12]. CBNAAT of Broncho-alveolar Lavage (BAL) looks convincing as a good diagnostic method for the purpose of early diagnosis or ruling out pulmonary tuberculosis [13]. In India, a high TB burden country there is scarcity of literature regarding Mycobacterium Tuberculosis / Rifampcin assay in Bronchoalveolar lavage fluid for diagnosis of pulmonary tuberculosis. Therefore this study was planned to assess diagnostic utility of Cartirage based nucleic acid amplification test in Brochoalveolar lavage fluid for early diagnosis of pulmonary tuberculosis in sputum smear negative pulmonary tuberculosis cases in a tertiary care settings and compared it with traditional mycobacterial culture.

MATERIAL & METHODS

This study was a hospital based cross sectional study, done at respiratory medicine department of tertiary care centre of north India, between a period of February 2017 to February 2020. Ethical clearance was taken from the institutional ethical committee.

Patients age above 18 years of either sex, who were clinically and radiologically pulmonary TB suspect and sputum smear negative for acid fast bacilli and whom alternative diagnosis was ruled out were included in the study.

Those patients who were not willing to participate in study and critically ill and not fit for bronchoscopy procedure (like having coagulation disorders, refractory hypoxia, severe thrombocytopenia, cardiovascular instability, and severe pulmonary hypertension) were excluded. Those patients of smear positive pulmonary tuberculosis, Extra Pulmonary Tuberculosis and who had received more than 2 weeks of anti-tubercular therapy in the last 3 months and human immune deficiency virus infected patients were also excluded from the study. Those patients (n=147) who fulfilled the inclusion and exclusion criteria were recruited in the study. Data were collected from patients according to a predesigned proforma gathering clinical history and examination, as well as the results of routine investigations (Complete Blood Count, Liver Function Tests, Kidney Function Tests, Random Blood Sugar, Fasting and Post Prandial Blood Sugar), Chest X-ray, High Resolution Computerized Tomography Scan and Sputum smear Microscopy (Fluorescent) for Acid Fast Bacilli and results of bronchial aspiration fluid which was sent for CBNAT and MGIT.

Data were analysed using SPSS software (SPSS Inc. Statistics for Windows, Version 26.0). All data were expressed in percentage, proportions, mean, and standard deviation (SD). Sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Values (NPV) were calculated.

RESULTS

Volume 4, Issue 1; January-February 2021; Page No 17-22

The mean age of the patients in this study was 43.7 ± 16.8 years with a range from 18 to 70 years. There were 35.37 % of patients found in the age group of 40-50 years which was most common age group.There were 82 (55.78%) males and 65 (44.22%) were females. Maximum patients i.e. 86 (58.50 %) belonged to lower class.

The most common presenting symptom was cough with or without expectoration in 147 (100%) followed by fever 138 (93.88%), breathlessness 50 (34.01%) and haemoptysis in 45 (30.61%) patients.

The most common finding on chest radiograph was nodular opacities in 34% patients followed by cavity 21%, cavity and nodule 19%, consolidation (10%), cavity and consolidation (11%), fibrosis and bronchiectasis in (5%). Overall bilateral involvement was seen in 42% of patients followed by right sided involvement (33%), 25% of the patients had left sided involvement in chest x-ray.

In this study diabetes mellitus was found in 29 (19.72%) patients , and detection of mycobacterium tuberculosis infection among diabetic patients by CBNAAT in 18 (62.06%) patients and by MGIT in 11 (37.93%) patients respectively. (Table.1)

In this study CBNAAT was found positive in 70 (47.61%) patients (Figure 1) and out of 70 patients Rifampicin resistance was detected in 09 (12.88%) patients. MGIT was found positive in 58 (39.45%) patients and Non tuberculous mycobacteria (NTM) was found in 13 (8.84%) patients.(Table.2) The Sensitivity, Specificity, Positive Predictive Value and Negative predictive value of CBNAAT to detect Mycobacterium tuberculosis in BAL fluid of sputum smear negative pulmonary tuberculosis patients in comparison with MGIT as the gold standard were 86.20%, 73.68%, 71.42% and 87.50% respectively.

DISCUSSION

In this study mean age of the patients was (43.7 ± 16.8) years comparable to study done by Dwari A K et al 2018 [14] .We found male (55.78%) prepronderance in our study , similar findings also reported by studies of Gowda et al 2018, Agarwal A et al. 2018 [15,16]. The predominant symptoms noted observed in study were cough (100%) and fever (93.88%), similar findings also observed by other studies as well [15,16].

The most common lesions detected by chest imaging were nodular opacities (34%) followed by cavity (21%), cavity and nodule (19%), Cavity and consolidation (11%), consolidation (10%), fibrosis and bronchiectasis (5%). Overall bilateral involvement was seen in 42% of patients followed by right sided involvement (33%), 25% of the patients had left sided involvement in chest x-ray similar findings also supported by other previous studies [16,17] . In our study out of 147 sputum smear negative pulmonary tuberculosis patients, CBNAAT was found positive in BAL fluid by detecting Mycobacterium tuberculosis in 70 (47.48%) patients, while MGIT was found positive for Mycobacterium tuberculosis in 58 (39.45%) patients and Rifampicin resistance was found in 9 (12.88%) patients among those patients detected positive by CBNNAT. Nontuberculous mycobacteria (NTM) was detected in 13(8.44%) patients. Similar findings were reported in various previous studies [15,16].

In this study the Sensitivity, Specificity, Positive predicted value and Negative predictive value of CBNAAT with culture (MGIT) as a gold standard in BAL fluid of sputum smear negative pulmonary tuberculosis patients were 86.20%, 73.68%, 71.42% and 87.50% respectively, which was found statically significant ($p < 0.001$), these findings were comparable with other previous studies [15,16,18].

CONCLUSION

In this study the sensitivity, specificity, positive and negative predictive value of CBNAAT with Culture (MGIT) in BAL of sputum smear negative pulmonary tuberculosis patients were 86.20%, 73.68%, 71.42% and 87.50% respectively. Therefore CBNAAT in BAL can be used to confirm the early diagnosis of pulmonary tuberculosis in sputum smear negative pulmonary tuberculosis cases and due to rapidity and ability to detect rifampicin resistsance simultaneously, it will be further useful to dealt with such cases of drug resistance without undue delay .

Limitation

Our study was based exclusively on patients attending our department, so results are not representative of whole community. Treatment outcomes were not studied in this study

REFERENCES

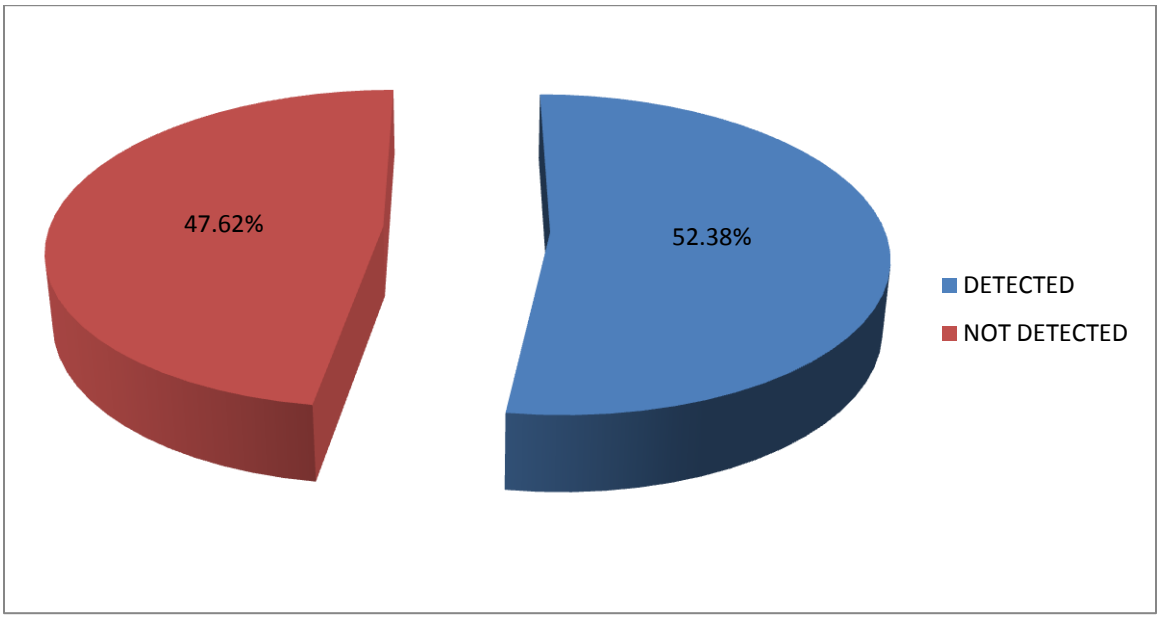
Volume 4, Issue 1; January-February 2021; Page No 17-22

1. World Health Organization. Treatment of Tuberculosis: Guideline National programmes. Accessed on 1/10/2018. Available from : http ://www.who.int/tb/en.
2. TB India 2007. RNTCP Status Report. New Delhi: Central TB Division, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India. Accessed on 1/10/2018. Available from: htpp: // www.tbcindia.nic.in/.
3. Kvale PA, Johnson MC, Wroblewski DA. Diagnosis of tuberculosis: routine cultures of bronchial washings are not indicated. Chest.1979; 76(2):140-142.
4. Bhaglani DK, Sarkar malay, Singh digvijay, Negi RS, Sharma S. Role of fiber-optic bronchoscopy in sputum smear negative pulmonary tuberculosis. NJMR. 2016; 6(2): 134-39
5. Fujii H, Ishihara J, Fukaura A et al. Early diagnosis of tuberculosis by fiberoptic bronchoscopy. Tubercle Lung Dis.1993; 73: 167–9.
6. Chan HS, Sun AJ, Hoheisel GB. Bronchoscopic aspiration and bronchoalveolar lavage in the diagnosis of sputum smear-negative pulmonary tuberculosis.Lung.1990; 168(4): 215-20.
7. Sharma SK, Pande JN. Fiberoptic bronchoscopy. Indian J Chest Dis Allied Sci.1988; 30(3):163-5.
8. Reynolds HY. Bronchoalveolar lavage. Am Rev Respir Dis. 1987 Jan; 135(1):250-63.
9. Walters EH, Gardiner PV. Bronchoalveolar lavage as a research tool. Thorax. 1991; 46(9):613-
10. Shah I, Gupta Y. Role of molecular tests for diagnosis of tuberculosis in children. Pediatric Oncall Journal. 2015; 12(1): Accessed on 1/10/2018. Available at: www.pediatriconcall.com/Journal/Article/
11. World Health Organization: Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance:Xpertmtb/rifsystem.Policystatement2011.http://whqlibdoc.who.int/publications/2011/9789241501545_eng.pdf
12. WHO Policy statement: Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF system. Geneva: World Health Organization; 2011. Accessed on 4/10/2018. Available at: http://www.who.int/iris/handle/10665/44586
13. Mohan A, Sharma SK. Fiberoptic bronchoscopy in the diagnosis of sputum smear- negative pulmonary tuberculosis: current status. Indian J Chest Dis Allied Sci. 2008; 50: 67–78.
14. Dwari Amiya Kumar, Jha Sumanta, Haldar Dibakar , Biswas Bisanka , Saha Sanjay Kumar. CBNAAT co-testing for suspected TB. Journal of Clinical and Diagnostic Research. 2018; 12(6): 22-24.
15. Gowda NC, Ray A, Soneja M, Khanna A, Sinha S. Evaluation of Xpert® *Mycobacterium tuberculosis*/rifampin in sputum-smear negative and sputum-scarce patients with pulmonary tuberculosis using bronchoalveolar lavage fluid. Lung India 2018; 35: 295-300.
16. Agarwal A, Pandey S,Verma SK, Verma A, Raza T, Kant S. Comparison of realtime PCR with phenotypic methods in bronchoalveolar lavage in diagnosis of sputum smear negative pulmonary tuberculosis patients. Int J Res Med Sci 2018; 6:1694-8.
17. Avashia S, Choubey S, Mishra S, Kharate A, To study the usefulness of CBNAAT (Cartridge Based Nuclear Acid Amplification Test) in BAL (Bronchoalveolar Lavage) Samples In The Diagnosis Of Smear-Negative / Non Sputum Producing Patients With Suspected Tuberculosis. J Evolution Med Dent Sci. 2016; 5(1): 55-59.
18. Lee HY, Seong MW, Park SS, Hwang SS, Lee J, Park YS, *et al*. Diagnostic accuracy of Xpert® MTB/RIF on bronchoscopy specimens inpatients with suspected

Volume 4, Issue 1; January-February 2021; Page No 17-22

pulmonary tuberculosis. Int J Tuberc Lung Dis 2013; 17: 917-21.

Figure 1: Detection of Mycobacterium tuberculosis in BAL fluid by CBNAAT (N=147)



CBNAAT* Cartirage Based Nucleic Acid Amplification Test, BAL Bronchoalveolar Lavage**

Table 1: Characteristics of Sputum Smear Negative TB Patients

S/N	Characteristics	Number Of Patients
		N= 147 (%)
1	**Demographic Characteristics**	
	Age in years (Mean ± SD)	43.8 ± 16.7
	Sex	
	Male	82 (55.78)
	Female	65 (44.22)
2	**Clinical Characteristics**	
	Smoker	58 (39.90)
	Non Smoker	89 (60.54)

Volume 4, Issue 1; January-February 2021; Page No 17-22

	Symptoms	
	Cough	145(100)
	Fever	138(93.88)
	Breathlessness	50(34.01)
	Haemoptysis	45(30.61)
	Chest X-ray Presentation	
	Nodular Opacities	49(33.33%)
	Cavity	30(20.40)
	Cavity and Nodules	28(19.04)
	Cavity & Consolidation Consolidation	17(11.56) 15(10.20)
	Bronchiectasis	8(5.44)
	Diabetes	29(19.72)
	Previous History Of Tuberculosis	49(33.34)

TABLE 2: Comparison of CBNAAT and MGIT in BAL of Sputum Smear Negative Pulmonary Tb Patients

CBNAAT	**MGIT**		**Total**
	POSITIVE	**NEGATIVE**	
POSITIVE	50	20	70
NEGATIVE	08	56	64
Total	58	76	134

CBNAAT* Cartirage based nucleic acid amplification test, MGIT** Mycobacterium Growth Indicator Tube ***Nontuberculous Mycobacterium was found in 13 patients.

Volume 4, Issue 1; January-February 2021; Page No 17-22