Original Research Article

Role of cartridge based nucleic acid amplification test in bronchoscopy guided bronchial wash specimens in sputum smear negative PTB patients attending government general hospital, Kakinada

Potla Harika¹, Kiran Mathangi¹,*, K Chakravarthi¹, K. Rajendra Kumar¹

¹Dept. of Pulmonary Medicine, Rangaraya Medical College, Kakinada, Andhra Pradesh, India

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A B S T R A C T

Introduction: Tuberculosis is a global health burden still causing large mortality and morbidity. According to WHO's 2018 Global TB Report two main routes for reducing TB incidence and death are - diagnosis and treatment. The main challenging issue with TB is to obtain a rapid and accurate diagnosis for initiating early treatment. Sometimes patient with active pulmonary tuberculosis fail to produce adequate sputum resulting in increase of false-negatives. Sputum-smear negative pulmonary tuberculosis is highly infectious and remains a diagnostic challenge. Fiber-optic bronchoscopy is an important tool for early detection and confirmation of sputum smear-negative and sputum-scarce PTB as it provides high-quality biological samples like bronchoalveolar lavage (BAL) fluid. The aim of the present study was to evaluate role of in Gene Xpert MTB/RIF on bronchoscopic specimens in sputum smear negative patients with suspicion of PTB.

Materials and Method: A prospective observational study was done on 100 patients with clinical suspicion of PTB who either have a negative sputum smear microscopy or unable to produce qualitative sputum attending outpatient and admitted in Pulmonology department, Government General Hospital, Kakinada.

Results: Out of 100 patients, 47 were diagnosed and confirmed as pulmonary tuberculosis of which bronchial specimens smear positive were 5(10.6%), bronchial specimens smear negative but CBNAAT positive were 42(89.3%). At last as CBNAAT has dual diagnostic advantage of detecting rifampicin resistance, about 5 cases were detected as rifampicin resistance.

Conclusions: CBNAAT/RIF assay on BAL specimen provides an accurate diagnosis of PTB in patients with sputum smear negative results or those who cannot expectorate sputum and superior to sputum smears in detecting rifampicin resistance.

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1. Introduction

Tuberculosis is a global health burden¹. Though it is treatable, its mortality is high. According to WHO: Sputum for AFB is the mainstay of diagnosis with sensitivity 66-77%. Sputum positivity requires millions of bacilli. In paucibacillary cases even though clinical and radiological features are suggestive of Tuberculosis, majority of sputum smear examinations are associated with negative results. Bronchial washings and post bronchoscopic sputum collected by fibreoptic bronchoscopy may provide a confirmative and early diagnosis in such patients with the help of CBNAAT.

Gene (CBNAAT) is rapid, sensitive and specific not only for acid fast bacilli detection but also for rifampicin resistance which is a surrogate marker for multidrug resistant TB. Gene Xpert should be used in all sputum smear negative pulmonary tuberculosis cases where conventional diagnostic tests are less sensitive and more time consuming.
2. Aims and Objectives

To assess role of Gene Xpert (CBNAAT) in bronchoscopy guided bronchial wash specimen in sputum smear negative pulmonary tuberculosis.

3. Materials and Methods

1. 100 patients with clinical suspicion of PTB who either have a negative sputum smear microscopy or who were unable to produce qualitative sputum, selected from outpatient and inpatient in Department of Pulmonary medicine, Government general hospital, RMC, Kakinada from November 2018 to November 2019.

2. In these patients fibre optic bronchoscopy was performed after taking consent and their bronchoscopic specimens sent for gene Xpert MTB/RIF assay and for AFB smear.

3.1. Inclusion criteria

1. Patients with clinical suspicion of PTB based on symptoms like cough for more than two weeks, Hemoptysis, evening rise of temperature, asthenia, loss of weight and loss of appetite.

2. Radiological features suggestive of pulmonary tuberculosis who have a negative sputum smear microscopy or who were unable to produce qualitative sputum.

3.2. Exclusion criteria

1. Sputum positive cases, isolated extrapulmonary tuberculosis ,HIV positive patients and patients not fit for bronchoscopy procedure e.g. those having refractory hypoxemia, bleeding disorders, cardiovascular instability, status asthmaticus and marked hypercapnia.

2. Patients not given consent for bronchoscopy

3.3. CBNAAT

The WHO recommended, this test should be used as initial diagnostic test in individuals suspected of having MDR TB, and HIV associated TB. They also suggest that it could be used as an follow up test to microscopy in settings where MDR TB and HIV is of lesser concern, especially in the smear-negative specimens, because of lack of accuracy of smear microscopy. The Gene x-pert MTB/RIF cannot be used as treatment monitoring, as it detects both live and dead bacteria.

The main advantage is identifying rifampicin resistance, is again the matter of speed. Normally to get any drug resistance, the result takes weeks rather than hours.

3.4. Bronchoscopy

Dr. Shigeto Ikeda\(^3\) established the standards for the first flexible bronchoscope.

The flexible bronchoscopes and their performance have continuously improved over the years. The flexibility, ease of manipulation, simplicity of use which permits rapid examination under topical anaesthesia has made flexible bronchoscope the primary endoscopic procedure in pulmonary diseases\(^4\). The flexible bronchoscopes vary from ultrathin for neonatal endoscopy to larger adult size therapeutic devices. Thin flexible bronchoscopes allow bronchoscopist to directly visualize 8 to 12 generations of bronchi. Ultrathin flexible bronchoscope has an outer diameter of 1.8 mm. The effective length of the thin bronchoscope is 1150 mm and its total length is 1350 mm. It is designed to allow direct observation of 2 to 30 mm sized objects within a range of 75 degrees. The small size of the ultrathin bronchoscope allows them to be introduced through the 2.6 mm channel of conventional flexible bronchoscope.

3.5. Bronchoscopic techniques used

3.6. Bronchoalveolar lavage

Bronchoalveolar lavage enables sampling of the distal airways and alveolar spaces\(^5\).\(^5\).

3.7. Bronchial washings

Bronchial washings allow targeted sampling of proximal or segmental airways. The bronchoscope is held proximal, but close, to the site of abnormality. About 10–20 mL aliquots of saline are instilled and aspirated back. The sensitivity of bronchial washings is very variable.

4. Results

1. The study group consists of 100 patients of which 62 (62%) are males and 38 (38%) are females. The predominant age group in the study is 41-60(41%) followed by 21-40 (32%). Study group have more males and females in the age group of 41-60 years,least in the age group18-20 yrs.

2. Predominant symptom is cough which is seen in 80% of patients followed by Fever (60%), loss of appetite with significant weight loss(45%),night sweats (26%) and hemoptysis (12%).

3. Radiological features suggestive of PTB(20%).Most common radiological presentation is consolidation (50%)followed by fibro cavitory lesions (35%), normal chest X-ray (13%), Mediastinal lymphadenopathy (2%).

4. Comorbid conditions such a Diabetes mellitus in 25 cases (25%) and CKD in 1 case (1%) , chronic alcoholism seen in 40 cases (40%) and patients on
steroid therapy were 10 (10%).

5. Out of total 100 patients selected, 80 patients were sputum smear negative and 20 patients were unable to produce sputum.

6. The study group out of total 47 positive cases, more positives came in Bronchial washings- 27 cases (57.44%) followed by Post bronchoscopic sputum and BAL both came to be 10 positive each (21.27%).

7. In present study, out of total 47 positives- 42 were CBNAAT positive and 5 were AFB smear positive. 18 patients were both BAL smear positive and CBNAAT positive. 37 patients (88%) are Rifampicin sensitive and 5 patients (11.9%) are Rifampicin resistance.

5. Discussion

The study performed in 100 patients with a high pre-test probability for pulmonary Tuberculosis. Present study having 62% males comparable to Uppe et al., study (60.5%), Chukka et al., study (62.96%) and Gowda et al., study (60%). Mean age in the study group males 43.20 and females 43.5 comparable to Chukka et al., study in which males 48.91 and females 44.12 and Hazarika et al., study in which males 42.7 and females 41.6. In general TB incidence is more common in extremes of age group that is adolescents and elderly group. But the present study and other studies suggests PTB effecting middle age group, who have highest work efficiency. This is because of presence of comorbidities like DM, CKD, Chronic alcoholism and steroid therapy in the middle age group in the present study. So, this is the reason why the case finding of PTB is essential in a community. In symptomatic suspected cases of PTB if sputum smear is not diagnostic, then these are the individuals that suffer and also spread the disease in the society.
The present study consists of 50% patients presenting with non-resolving pneumonia comparable to Gowda et al., study and Chakradhar et al., study. In general, PTB presenting as pneumonia is more common in children and rare in adult population. Hence there is more chance of under diagnosis of PTB in adult population presenting with consolidation. As India is an endemic country for PTB, it is important to suspect all cases of non-resolving pneumonia to Bronchoscopy. Bronchoscopy also identifies any endobronchial obstruction, foreign body, mucus plug or any tumor that results in non-resolving pneumonia.

In the present study, a total of 100 clinico-radiological suspects of PTB are subjected to Bronchoscopy and Bronchoalveolar specimens are sent for AFB smear and CBNAAT simultaneously. Total positives were 47 out of 100 patients. Out of 47 positive patients, 23 were bronchial specimen AFB positive with a sensitivity of 42.85% and 42 patients were CBNAAT positive with a sensitivity of 78.26%. Out of 23 AFB positive patients, 18 patients were both AFB and CBNAAT positive and 5 were only AFB positive.

The sensitivity of bronchial specimens ZN stain and CBNAAT are 48.86% and 78.89% respectively in Hazarika et al., study. In Uppe et al., study, the sensitivity of bronchial specimen ZN stain and CBNAAT are 76.83% and 84.15% respectively. In Khalil et al., study, the sensitivity for BAL ZN stain and CBNAAT are 39.53% and 91.86% respectively. The present study along with other studies show that Gene X-pert have more sensitivity when compared to ZN stain.

In the present study, AFB smear and CBNAAT performed in the bronchial specimens. To conclude its better to consider all clinic-radiological suspects of PTB for bronchoscopy and bronchial specimens should be sent for both AFB and CBNAAT simultaneously. So, that it gives better total positivity rate of PTB. Finally, gold standard test is culture method but it takes nearly 6-8 weeks for obtaining results.

6. Conclusions

To conclude, Bronchoscopy is useful tool in early diagnosis of smear negative PTB in tertiary care centers like teaching hospitals. In resource-limited settings and less accessible areas where sophisticated lab for culture and DST is difficult, X-pert MTB/RIF provides a vaible option. In sputum-smear negative and sputum-scarce patients with clinic-radiological features suggestive of active PTB, Gene X-pert has a high sensitivity compared to AFB smear for diagnosis in Bronchial specimens. Also Gene X-pert detects very early within 2 hours compared to cultures which remain the gold standard test for diagnosis of PTB, but takes very long time for results. Gene X-pert has an added advantage of detection of Rifampicin resistance.

7. Acknowledgement

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8. Conflict of Interest

None.

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None.

References


Author biography

Potla Harika Post Graduate
Kiran Mathangi Assistant Professor
K Chakravarthi Assistant Professor
K. Rajendra Kumar Professor and HOD