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Research Article

Role of Fibreoptic Bronchoscopy in Smear Negative Re-Treatment Pulmonary Tuberculosis

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Abstract

Introduction: Tuberculosis in India continues to remain a socioeconomic burden. The disease incidence and prevalence have considerably decreased in the recent times, due to the effective implementation of the national programme. However, the smear negative tuberculosis continues to pose threat to the diagnostic and management of the clinicians. This study was done to evaluate the role of Fibre Optic Bronchoscopy in detection of Acid Fast Bacilli in Smear Negative Tuberculosis.

Methodology: A cross sectional study was done among 52 patients with smear negative tuberculosis visiting the tuberculosis center in Chennai. Bronchial wash and brush was done and samples were analysed for AFB using Zeihl- Neelson technique, culture sensitivity using LJ medium and cytology. Line Probe Assay was also carried out among the study participants.

Results: Bronchial wash showed 27% positivity by smear examination and 44% positivity by culture method. The study also revealed 2 patients with carcinoma by cytology. On comparison with Line Probe Assay, Fibre Optic Bronchoscopy showed statistical significant results of detection ($p<0.05$).

Conclusion: Fibre Optic Bronchoscopy is an effective tool in detection of smear negative tuberculosis and will help in early diagnosis and prevention of secondary infections.

Keywords: Bronchoscopy; Line probe assay; Smear negative tuberculosis

Introduction

Tuberculosis (TB) is a highly infectious bacterial disease caused by *Mycobacterium tuberculosis*. Various parts of the body are affected by the disease. Pulmonary Tuberculosis is the commonest form of TB. Usually TB bacillus spreads through air, as a droplet infection. The life time risk of developing tuberculosis in these infected people is 10% [1]. About 10-15 healthy persons are infected by a smear positive pulmonary tuberculosis patient in the general population in a year and if these smear positive patients are left untreated, they remain infectious for 2 to 3 years [1].

In 2012, globally estimated TB incident cases was about 8.6 million, it was equivalent to 122 cases per One Lakh Population. The absolute number of incident cases is falling slowly. In 2012 most of the estimated number of cases occurred in African Region (27%) and the Asia (58%) [2]. Two smaller proportions of cases occurred in the European Region (4%), the Eastern Mediterranean Region (8%) and the Region of the Americas (3%). In 2012 the largest number of incident cases occurred in five countries including China (0.9-1.1 million), India (2.0-2.4 million), Pakistan (0.3-0.5 million), South Africa (0.4-0.6 million) and Indonesia (0.4-0.5 million). Among the 8.6 million incident TB cases in 2012 globally, people living with HIV was estimated to be around 1.0-1.2 million (12-14%). About 450000 (Range: 300000 to 600000) new cases of MDR-TB were estimated worldwide by end of 2012. This total included acquired and primary MDR-TB cases [2].

In 2012 estimated prevalence TB cases was 12 million (Range: 11-13 million). It was equivalent to 169 cases per one lakh Population. The prevalence rate had reduced by 37% globally from 1990 to the end of 2012 [2]. In 2012, TB deaths were an estimated 1.3 million, of which 3.2 Lakh deaths occurred in HIV-positive people (TB deaths occurred in HIV-positive patients were classified as HIV deaths in ICD-10). Among the total deaths, 4.1 lakh deaths occurred in women and 74,000 occurred in children. The deaths from MDR-TB included approximately 170000.

In total TB deaths, approximately 75% occurred in the South-East Asia and African Regions in 2012. One-third of global TB deaths occurred in India and South Africa. Globally in 2012 the number of TB deaths per 100,000 populations averaged 13 and the same was 17.6 when TB deaths among HIV-positive patients were included [2].

In India, one fourth of the global incidence TB cases occur annually. Globally, annual incidence of TB cases was estimated about 8.6 million by the end of 2012, in which 2.3 million TB cases was estimated to have occurred in India [3].

The burden of tuberculosis is considerably reduced in India, owing to the Revised National Tuberculosis Control Programme. Compared to 1990, TB mortality rate had reduced by 42% in 2012. Similarly compared to 1990, TB prevalence rate had reduced by 51% in 2012. Tuberculosis prevalence per 100,000 populations had reduced to 230 in 2012 from 465 in year 1990. In exact numbers, prevalence has reduced from 40,00,000 to 28,00,000 annually [3].

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Pulmonary tuberculosis is commonly diagnosed by sputum smear examination. Sputum microscopy is a low cost, high specificity test. It is an essential component of the DOTS strategy of the World Health Organization. But not all patients with clinical picture of tuberculosis reveal acid fast bacilli in their sputum. In 22% to 61% of the patients smear negative - culture positive is observed [4-6].

Sputum smear negative pulmonary tuberculosis still remains common problem, particularly in retreatment patients. They continue to be a source of infection to the community, if there is a delay in diagnosis and treatment of these patients.

In our study we used the Fibre-Optic Bronchoscopy (FOB) as a primary tool for diagnosis of smear negative retreatment pulmonary tuberculosis as early treatment renders those patients non infectious, interrupts the transmission of TB and reduces the incidence of MDR-TB in those patients.

Objectives

1. To evaluate Fibre-Otptic Bronchoscopy as a diagnostic tool in smear negative retreatment pulmonary tuberculosis.

2. To compare pre FOB sputum LPA with Bonchial wash AFB culture by LJ medium.

Methodology

Study design

This study was carried out as a cross sectional study.

Study area

The study was carried out in Government Hospital of Thoracic Medicine (GHTM), Tambaram Sanatorium.

Study population

The study population comprised of patients with clinical and radiological suspicion of pulmonary tuberculosis with 2 sputum smears negative for AFB, and who had already taken anti tubercular treatment.

Study period

The data was collected during the period from December 2013 to July 2014.

Inclusion criteria

Patients taken anti tuberculous treatment for more than one month (include defaulter and cured patients).

Clinical and radiological features suggestive of active tuberculosis but sputum for AFB smear negative.

Exclusion criteria

New smear positive TB

Smear positive retreatment tuberculosis

Patients with respiratory failure

Patients who are not willing to participate in the study

Patients who are not fit for FOB

Sample size and sampling

All the eligible patients with sputum negative tuberculosis who visited the center during the period between December 2013 and July 2014 were taken up for the study. A total of 52 participants were included. The sampling technique used was convenience sampling.

Tool for data collection

The study is a prospective study.

1. Recruitment of patients as per inclusion criteria

2. Thorough clinical examination

3. Symptoms duration

4. Anti-tuberculous treatment history

5. Chest radiograph

6. Sputum for AFB staining, LPA

7. FOB-Bronchial wash /brush at suspected area of lesion

Data collection

The study participants were evaluated for the fitness for FOB with blood investigations which included Complete Blood Count (CBC), Bleeding time, Clotting time, Electro Cardio-Gram (ECG), pulse oximetry, and cardiac evaluation. Fit patients were subjected to FOB, bronchial wash & brush from the suspected site.

Samples were analyzed by following method

Sputum Smear for AFB (pre and post FOB)

Bronchial wash for AFB smear and AFB culture

Bronchial wash for non-tuberculous culture and sensitivity

Bronchial brush for AFB smears

Bronchial wash and brush for cytology

Pre FOB sputum for LPA (if LPA was negative, culture was done by Solid and Liquid Media at National Institute for Research in Tuberculosis (NIRT), Chennai).

Statistical analysis

Data was entered and analysed using Statistical Packages for Social Sciences (SPSS) software ver.16. Chi square test was used to compare the results of FOB and Line Probe Assay.

Ethical clearance

Approval from the Institutional Ethics Committee was obtained prior to data collection. Informed consent was obtained from all the participants before commencement of data collection.

Results

A total of 52 participants between the ages 16 and 78 years participated in this study. The background characteristics of the study population are given in Table 1. Out of 52 participants, 92% were males and 8% were females.

The findings of bronchial wash for AFB smear by Zeihl-Neelsen method, culture and cytology are given in Table 2. While 27% recorded positive results by Zeihl-Neelson method, 44% were positive for AFB by culture. Moreover, 77% of the cytology reports showed acute inflammation.

Table 1: Background characteristics of the study participants.

S. No.	Characteristics	Frequency (N=52)	Percentage (%)
1	**Sex**		
	Males	48	92
	Females	4	08
2	**Number of treatment episodes**		
	One	37	71
	Two	15	29
3	**Treatment outcome**		
	Cured	24	46
	Defaulter	28	54

Table 2: Findings of Bronchial wash among the study participants.

S. No.	Findings	Frequency (N= 52)	Percentage (%)
1	**AFB smear by Zeihl-Neelson method**		
	Negative	38	73
	Positive	14	27
2	**AFB by culture in LJ medium**		
	Negative	29	56
	Positive	23	44
3.	**Cytology findings**		
	Acute Inflamatory Pathology	40	77
	No Specific Pathology	8	15
	Acellular Smear	4	8
4	**Bacterial C/S**		
	No growth	40	77
	Pseudomonas	4	7
	Streptoccus pyogenes	3	6
	Klebsiella	2	4
	Staphaureus	2	4
	Moraxella	1	2

The findings of bronchial brush are given in Table 3. While 24% were positive for AFB by smear examination, 71% showed acute inflammation in cytology. Moreover, assessment of secondary infections showed that 7% were positive for Pseudomonas and 6% were positive for *Streptococcus pyogenes*. Moreover, post FOB sputum for AFB was positive among 12% of the participants.

The findings of bronchial wash for AFB smear by Zeihl-Neelsen method, culture and cytology are given in Table 2. While 27% recorded positive results by Zeihl-Neelson method, 44% were positive for AFB by culture. Moreover, 77% of the cytology reports showed acute inflammation.

The comparison between pre-FOB LPA and bronchial wash findings are given in Table 5. The findings showed statistical significant result with FOB wash compared to pre-FOB sputum for LPA (p value <0.001).

Discussion

The WHO Expert Committee on Tuberculosis says that patients

Table 3: Bronchial brush findings among the study participants.

S. No	Findings	Frequency (N=52)	Percentage (%)
1	**AFB by Zeihl-Neelson method**		
	Negative	40	76
	Positive	12	24
2	**Cytology findings**		
	Acute inflamatory pathology	37	71
	No specific pathology	12	23
	Positive for malignancy	2	4
	Acellular smear	1	2

Table 4: Findings of Pre FOB Line Probe Assay among the study participants.

S. No.	Pre FOB sputum smear for AFB	Frequency (N=52)	Percentage (%)
1	Negative	37	71
2	Sensitive to INH, RIF	14	27
3	Resistant to INH, RIF	1	2

Table 5: Comparison of pre FOB sputum for LPA and bronchial wash AFB culture by LJ medium among the study participants.

S. No	Bronchial wash for AFB Culture	LPA PRE FOB Sputum		Total
		Positive	Negative	
1	Positive	14	9	23
2	Negative	1	28	29
	Total	15	37	52
	p value <0.001			

with pulmonary tuberculosis, whose disease has not been confirmed bacteriologically should be classified as "suspects" until the presence of AFB is demonstrated and a patient with persistent symptoms of tuberculosis, whose sputum does not contain AFB should be followed up and anti-tubercular treatment given only if the diagnosis confirmed by bacteriologically [7].

Published data suggest that over 50% of smear negative patients would need anti tuberculosis treatment by the end of 12 months if untreated [4,8]. Data from longitudinal survey from Bangalore, India, shows the mortality rate of smear negative, culture positive patients as 14.1% compared with the 34.7% of smear positive cases at the end of 18 month follow up. With the use of Fibre Optic Bronchoscopy (FOB), diagnosis of PTB in sputum smear negative retreatment patients has become possible. The advantage with this instrument was the ability to visualize the bronchial tree and collect samples directly from the abnormal bronchial site.

Even though FOB procedures have some risk of complications like hemoptysis & Pneumothorax, it was considered to be a relatively safe procedure [9]. In our study, no complications were observed.

A number of previous studies show that the positivity of Bronchial Aspiration (BA) varies from 13% to 61%. Danek et al. observed BA smear positive in 24% cases while So et al. obtained a positive yield of 38% in bronchial aspirate [10-14]. Anand reported the diagnostic yield of BA smear to be 28%, BA culture to be 32%.

In our study bronchial wash AFB smear positive in 26.92% cases (14/52) and bronchial wash for AFB culture positive in 44.23% (23/52).

Thus the data generated in our study is comparable to previous studies. In various other previous studies, Post bronchoscopy smear revealed AFB positivity ranging from 23% to 37%. Also, 21% was noted by Danek et al., 28% by Anand et al., 35% by Wallace et al., 23% by Kulpati et al. and 26% by Purohit et al. 37% by So et al. [12-15].

In our study post bronchoscopy sputum is positive in 11.53% (6/52). Bronchial brush for AFB smear is positive in 23% (12/52). In bronchial wash, Bacterial culture diagnosed 23% (12/52) pyogenic infections, Pseudomonas 4/12, Streptococcus pyogenes 3/12, Klebsiella 2/12, Staph aureus 2/12, Moraxella 1/12. Early treatment of these patients is necessary to prevent the spread of these infections in community. Bronchial wash cytology in 76.92% (40/52) and bronchial brush for cytology shows 71.15% (37/52) of acute inflammatory pathology. Importantly bronchial brush cytology shows malignancy in 2/52 patients (3.84%), in which one patient was diagnosed as adenocarcinoma, another patient was diagnosed as squamous cell carcinoma.

Pre bronchoscopy sputum for LPA detected M. tuberculosis in 15/52 (28.84%) patients of which 14 patients were sensitive to INH AND RIF, and one patient was diagnosed as MDR TB. Compared to pre FOB sputum for LPA (including LPA positive, culture positive) with FOB wash for AFB culture revealed better yield (p value<0.001) in the later group.

All pre FOB sputum for LPA positive patients (including culture positive) were within the margin of FOB wash for AFB culture positive patients, except one patient whose pre FOB sputum for LPA positive but bronchial wash for AFB culture negative. That is if FOB washes for AFB culture is negative, LPA of pre bronchoscopy sputum is also negative (LPA negative and culture negative) (p value<0.001) substantiating that fibreoptic broncoscopy is an excellent tool for diagnosis of smear negative pulmonary tuberculosis in retreatment patients.

Conclusion

The study concludes that flexible fibreoptic bronchoscopy is a useful tool in the diagnosis of sputum smear negative retreatment pulmonary tuberculosis patients. Bronchoscopy revealed a higher bacteriological confirmation of diagnosis in patients with strong radiological and clinical evidence suggestive of active pulmonary tuberculosis. Major advantage of bronchoscopy in smear negative retreatment pulmonary tuberculosis is, isolation of mycobacteria at an early stage when the destruction of lung parenchyma is minimal and the risk of spreading the disease to contact person can be decreased by early diagnosis and treatment. It also decides CAT II ATT in these patients, and it also diagnoses non tuberculous pathology like malignancy.

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