Original Research Article

A comparative study of CBNAAT and AFB smear for the diagnosis of sputum smear negative pulmonary tuberculosis patients in a tertiary health care centre of Southern Odisha

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A B S T R A C T

Background : Pulmonary tuberculosis (PTB) is one of the most common infectious diseases & Continues to be the major health problem even today. Sputum smear negative (SSN) pulmonary tuberculosis is about 40% to 60% of the clinical and radiological suspected cases of pulmonary TB. Establishing early diagnosis and starting treatment early can have significant effect on morbidity and mortality in these patients. Broncho alveolar lavage (BAL) was obtained by fibro optic bronchoscopy (FOB)

Objectives: Minimising the under and over use of anti-tubercular therapy in diagnosis of pulmonary TB. To compare between the sputum CBNAAT with BAL fluid CBNAAT , compare between sputum CBNAAT with BAL fluid AFB staining, compare between BAL fluid CBNAAT with BAL fluid AFB in diagnosis of SSN PTB.

Materials and Methods: 108 SSN patients with clinical and radiological findings of PTB were taken. BY FOB BAL obtained and subjected to CBNAAT. Sputum samples of the above patients were subjected to CBNAAT and compared.

Results: In this study commonest age group was 18 to 39 years;64 patients (59.25%). Males (57.40%) were more in numbers than females (42.59%). In our study, 24(25.92%) were alcoholic and 84 (90.72%) were non alcoholic. 68(73.44%) had co-morbid conditions. Out of them 28 (30.24%) were of obstructive airways disease which was the commonest co-morbidity. BAL CBNAAT Mtb detection was better than BAL AFB smear, sputum CBNAAT was significantly better than BAL AFB smear & BAL CBNAAT was better than sputum CBNAAT.

Conclusion: BAL CBNAAT is useful in the early diagnosis of sputum smear negative pulmonary tuberculosis cases

1. Introduction

Pulmonary tuberculosis represents an important worldwide public health problem. Tuberculosis (TB) is one of the top 10 causes of death worldwide which is known to be a communicable disease and it also ranks above(HIV/AIDS). About a quarter of the world's population is infected with M.tuberculosis and thus at risk of developing tuberculosis.[1] The goal of the National Strategic Plan is to achieve universal access to quality diagnosis and treatment for all TB patients in the community.[2] It has reawakened the importance due to increase in life expectancy in the population as absolute no of elderly have increased all over the world. India is one of the country having largest number of elderly persons above 60 years of age. Pulmonary tuberculosis is increasingly becoming more common in

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elderly age groups and hence World Health Organization in 1993 declared tuberculosis as a common infectious disease in the Indian subcontinent, as global emergency.

Rapid diagnosis of TB significantly decreases the lag time in initiation of treatment, thereby reducing transmission rates.[3] Cough of more than two weeks, fever of more than two weeks, significant weight loss, heamoptysis and any abnormality in chest radiographs are the few signs and symptoms of presumptive pulmonary tuberculosis cases. Mycobacterium tuberculosis, the causative organism for diagnosis of TB, requires various diagnostic tools like chest x-ray which has got its own limitations though it is more sensitive but less specific. Sputum microscopy is simple, inexpensive, got high specificity and high reliability, hence is key diagnostic tool for detection of pulmonary TB under RNTCP. But a variable range of about 40%-60%of patient's fail to produce sputum and remain smear negative. Diagnosis becomes difficult in those cases who remain sputum smear negative (SSN). Many patients are exposed to over diagnosis and over treatment with anti-tuberculardrugs. On the otherhand published studies suggest that more than 50% of smear negative patients would need chemotherapy if left untreated.[4] So other investigations are important in the diagnosis of sputum smear negative TB cases. Although mycobacterial culture is gold standard and most specific test for the diagnosis,it requires 3 to 8 weeks to grow. Therefore, this is not available to guide the initial therapy.[5] CBNAAT is a highly specific test as it uses three specific primers and five unique molecular probes to target the rpoB gene of Mycobacterium tuberculosis, which is a critical gene associated with rifampicin resistance.[6] It demonstrates suboptimal sensitivity in smear negative patients compared to conventional culture.[7] FOB (fiber optic bronchoscopy)usually used for the obtaining samples ofbronchoalveolar lavage, endobronchial biopsy, bronchial washing for diagnosis of sputum smear negative pulmonary tuberculosis patients.[8] More than 90% has been reported for diagnosing pulmonary tuberculosis by yield of bronchoscopy but cultures to be included in these cases for evaluating sputum smear negative pulmonary tuberculosis cases.[9,10] Hence in this study our objective is to minimisethe under and over use of anti-tubercular therapy in diagnosis of pulmonary TB.

So also to compare between the sputum CBNAAT with BAL fluid CBNAAT, compare between sputum CBNAAT with BAL fluid AFB staining , compare between BAL fluid CBNAAT with BAL fluid AFB in diagnosis of SSN PTB.

2. Materials and Methods

The hospital based cross sectional study was carried out in the Department of Pulmonary Medicine, in MKCG Medical College, a tertiary teaching hospital and referral unit insouthern Odisha during the period from February 2018 to January 2019. 108 patients attending to the RNTCP Clinic for sputum negative pulmonary tuberculosis, before starting ATT were included in the study based on the inclusion and exclusion criteria. Patients more than 18 years of age and a negative sputum smear for pulmonary tuberculosis were included. Patients who were sputum smear positive, who declined consent for FOB, having massive haemoptysis, cardiologicalsymptoms related to acute myocardial infarction or unstable angina, poorly controlled asthma or COPD and those having uncorrectable hypoxemia/hypercapnia or tracheal stenosis were excluded.

The data was recorded in a pre-designed case record form. The parameters recorded in the case record form included the basis of diagnosis of sputum smear negative pulmonary tuberculosis, radiological findings of the cases, sputum CBNAAT for M.tb detection and rifampicin resistance, AFB smear in BAL fluid study and M.tb detection, CBNAAT of BAL fluid for M.tb detection and rifampicin resistance and FOB related complications. The laboratory register maintained at RNTCP clinic was the primary data source for sputum AFB report radiological investigation reports and fiber-optic bronchoscope and CBNAAT report.

3. Results

108 sputum smear negative pulmonary tuberculosis patients were included in the study. The commonest age group was between 18 to 39 years. Out of 108 patients 62 were male and 46 were female (57.40%) and (42.59%) respectively.50patients (54%) were smokers, 20(21.6%) were former smokers and 38 (41.04%) were non-smokers. 34(36.72%) had more than one co-morbid conditions.28 (30.24%) cases had obstructive airway diseases and it was the commonest co-morbidity found. [Table 1] Predominant symptoms were cough, expectoration, fever and loss of appetite in that order M.tb detection by sputum CBNAAT method had a significantly higher positivity ratethan CBNAAT and AFB smear of BAL. Infiltration was thecommonestradiological patternfound in BAL CBNAAT positive cases. Multiple radiological pattern were associated with M.tb detection by sputum CBNAAT, BALCBNAAT and BAL AFB smear. [Table 2] Upper zone was the commonest zone associated with M.tb detection by sputum CBNAAT and BAL AFB smear. There was no history of prior anti-tubercular therapy or rifampicin resistance in cases with positive sputum CBNAAT and BAL CBNAAT and BAL AFB smear.[Table 3] BALCBNAAT M.tb detection was better than BAL AFB smear, sputum CBNAAT was significantly better than BAL AFB smear and BAL CBNAAT was better than sputum CBNAAT. FOB related complications are very minimal. [Table 4]

Table 1: Socio-demographic profile of sputum smear negative pulmonary TB patients

Socio-demographic Characteristics	Number	Percentage
Age in years		
18-39 years	64	69.12
40-59 years	30	32.4
60 and above	14	15.12
Sex		
Male	62	66.96
Female	46	49.68
Locality		
Urban	48	51.84
Rural	60	64.8
Addictions		
Alcoholics	24	25.92
Non alcoholics	84	90.72
Smoking		
Smokers	50	54
Former smokers	20	21.6
Non smokers	38	41.04
Comorbid conditions		
Diabetis mellitus	12	12.96
Chronic liver diseases	14	15.12
Obstructive airway diseases	28	30.24
PLHA	20	21.6
More than one comorbid condition	34	36.72

Table 2: Presence or absence of comorbid condition in relation to BAL CBNAAT, BAL AFB SMEAR, Sputum CBNAAT.

Co-morbid condition	BAL CBNAAT MTb detected	BAL CBNAAT MTb not detected	BAL AFB smear MTb detected	BAL AFB smear MTb not detected	Sputum CBNAAT MTb detected	Sputum CBNAAT MTb not detected
Present	48 (44.4%)	13 (12.03%)	14 (12.96%)	52 (48.14%)	30 (27.78%)	28 (25.92%)
Not present	28 (25.92%)	19 (17.60%)	2 (1.85%)	40 (37.03%)	10 (9.25%)	40 (37.03%)

Table 3: Relation of prior ATT history and Rifampicin resistance

Prior ATT history	Rifampicin resistance by BAL CBNAAT Detected	Rifampicin resistance by BAL CBNAAT Not Detected	BAL AFB Smear MTb detected	BAL AFB Smear MTb not detected	Sputum CBNAAT MTb detected	Sputum CBNAAT MTb not detected
Present	4 (3.70%)	26 (24.06%)	4 (3.70%)	18 (16.67%)	6 (5.56%)	16 (14.81%)
Absent	10 (9.25%)	68 (62.96%)	12 (11.12%)	74 (68.51%)	34 (31.48%)	52 (48.14%)

Table 4: Detection of MTb in Sputum CBNAAT, BAL AFB Smear and BAL CBNAAT

	MTb detected	MTb not detected
Sputum CBNAAT	40 (30.03%)	68 (62.96%)
BAL AFB smear	16 (14.81%)	92 (85.18%)
BAL CBNAAT	80 (74.07%)	28 (25.92%)

4. Discussion

108 sputum smear negative pulmonary tuberculosis patients were taken fulfilling the present study inclusion and exclusion criteria. In this study commonest age group was between 18 to 39 years. 64 patients out of n=108 (59.25%)which is almost equal to the age group of study by Agrawalla et al.[11] Out of 108 patients 62 were male and 46 were female(57.40) and (42.59%) respectively. Asper study of Nokbakhsh N et al which was FOB performed in sputum smear negative patients. The mean age was 52.6 years with a range of 20 to 76 years.[12] But that study was not an Indian study which was done in Northern Iran. It explains the mismatch for the age group in Indian population. Out of 47 patients 6(12.8%) were current smokers 13(27.7%)were ex smokers. 17(36.2%) cases were of regular alcohol consumers in a study which was conducted by Behera D et al.[13] Comorbidity conditions were found in 7(14.9%) cases. Out of 7 cases COPD was found in 4(57.1%) and diabetes mellitus in 2(28.6%). In our study 50(54%) were smokers, 20(21.6%) were former smokers and 38(41.04%) were non-smokers. 34(36.72%) had more than one co-morbid conditions. 28 (30.24%) cases had obstructive airway diseases and it was the commonest co-morbidity found. Main symptomatology of the patients were cough, expectoration, fever and loss of appetite which was consistent with the study of Gopathi N R et al.[14] In our study cough with or without expectoration present in almost 50% of cases. Mtb detection by sputum CBNAAT method is more significant rather than by BAL CBNAAT & BAL AFB smear. Infiltration was the commonest radiological pattern found in Mtb detection in BAL CBNAAT. Multiple radiological pattern associated with Mtb detection by sputum CBNAAT, BALCBNAAT and BAL AFB smear.

Upper zone was the most common zone which was associated with Mtb detection by sputum CBNAATand BAL AFB smear. No significant prior ATT history or rifampicin resistance was detectedby sputum CBNAAT and BAL CBNAAT and BAL AFB smear. BALCBNAAT Mtb detection is better than BAL AFB smear, sputum CBNAAT is significantly better than BAL AFB smear and BAL CBNAAT is better than sputum CBNAAT. FOB related complications are very minimal. Sofibre optic bronchoscopy (FOB) obtaining BAL is used to establish the diagnosis of PTB avoiding delay in treatment.[15]

Limitations of the study were of short duration. It is conducted in our health care system. So it may not be representative of the entire population of Southern Odisha. Culture for Mtb was not done so sensitivity, specificity and positive predictive value & negative predictive value of sputum CBNAAT, BAL AFB smear and BAL CBNAAT could not be calculated as culture was not done.

5. Conclusion

Most of our study population belongs to 18 to39 years of age group and male predominance is there. Obstructive airway disease is the most common co-morbid condition detected. Presence of this co-morbid condition is strongly associated with Mtb detection by sputum CBNAAT as compared to BAL and also CBNAAT and BAL AFB smear. Cough is the commonest symptom & more than one symptoms like fever, cough with expectoration and loss of appetite contributed CBNAAT is the most important method for diagnosis of sputum smear negative pulmonary TB

Mtb detection and rifampicin resistance detection can also be detected by this method. Sputum CBNAAT is better for Mtb detection than BAL AFB smear. BAL fluid CBNAAT is even better than sputum CBNAAT. Hence in sputum smear negative and also sputum CBNAAT Negative pulmonary tuberculosis cases, FOB can be done for early detection of Mtb in tertiary care hospitals.

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8. Conflicts of Interest

No conflicts of interest.

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