Original Research Article

Diagnostic yield of bronchoalveolar fluid/bronchoscopy among sputum AFB and CBNAAT negative presumptive tuberculosis patients: an observational study

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ABSTRACT

Background: Tuberculosis is one of the most common chronic infections globally, especially in developing countries like India and is a leading cause of morbidity and mortality. Therefore, early diagnosis, and microbiological confirmation of pulmonary TB is important to break the chain of transmission. This study was carried out to study usefulness of fiberoptic bronchoscopy in sputum smear negative and CBNAAT negative patient of presumptive tuberculosis.

Methods: It was an observational study in the Department of Respiratory medicine for duration of 2 years (Sept 2018- Aug 2020) among 100 adults cases of presumptive tuberculosis whose sputum were negative on sputum AFB and CBNAAT. Cases with relative or absolute contraindication for bronchoscopy were excluded from study.

Results: Mean age of study subjects was 47.31±12.29 years; M:F was 1.2:1 and 5% had past history of tuberculosis. Most common findings on chest X-ray was alveolar opacities (40%), inhomogeneous opacity (24%), cavitary lesions (20%), cystic lesion (8%) and fibrosis (6%) in different zones of lung. BAL sent for CBNAAT testing detected 15% mycobacterial TB, 2% mycobacterial TB with Rif resistance. Zn staining testing detected 10% AFB, on culture 14% showed AFB growth,4% had malignant cell findings. Diagnostic efficacy of Zn staining of BAL showed 42.86% sensitivity, 95.35% specificity, 60% PPV, 91.11% NPV and 88% diagnostic accuracy. BAL CBNAAT testing had 78.57% sensitivity, 93.02% specificity, 64.71% PPV, 96.39% NPV and 91% diagnostic accuracy. Most common complication was bronchospasm and hypoxia.

Conclusions: Fiberoptic bronchoscopy is useful investigation in establishing accurate and early diagnosis of lower respiratory tract infection.

Keywords: AFB, BAL, CBNAAT, Tuberculosis, Yield

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease usually caused by Mycobacterium tuberculosis (MTB) bacteria. It affects most of the organs in body. Most infections show no symptoms, in which case it is known as latent tuberculosis. About 10% of latent infections progress to active disease which, if left untreated, kills about half of that affected.[1]As of 2018 one quarter of the world's population is thought to have latent infection with TB.

New infections occur in about 1% of the population each year. In 2018, there were more than 10 million cases of active TB which resulted in 1.5 million deaths. This makes it the number one cause of death from an infectious disease. Globally it has affected 4-44% population in different continent of world.[2]

Current prevalence of TB in India making India the country with the highest TB burden. In 2015 out of estimated global annual incidence of 10.4 million TB

cases, 2.8 million were estimated to have occurred in India.[3] Presumptive pulmonary tuberculosis is cough for more than 2 weeks, fever for more than 2 weeks, significant weight loss, hemoptysis and abnormality in chest X ray.[3]

Detecting patients with active Pulmonary Tuberculosis (PTB) disease is an important component of Tuberculosis (TB) control as early appropriate treatment renders these patients non-infectious and interrupts the chain of transmission of TB. In tuberculosis diagnosis is based on isolation of organism from respiratory specimen specially sputum samples. WHO recommends bacteriological confirmation of pulmonary tuberculosis by detection of acid fast bacilli in respiratory specimen.[1]

Difficulties in diagnosis arises when a patient who is suspected tuberculosis clinically but doesn't produce sputum or who is sputum negative or sputum for CBNAAT negative. About 40-60 % of patient with active pulmonary tuberculosis suspected clinically fails to produce sputum or they are sputum smear negative, or CBNAAT negative.[4] Hence, more aggressive procedures need to be undertaken in these patients in order to establish the diagnosis.

Sputum induction is a relatively safe procedure with a good diagnostic yield. The various studies in this regard has reported variation in the diagnostic yield varying from 35 to 95%.[5,6] Along with sputum induction flexible bronchoscopy is commonly used for investigating patients with possible pulmonary tuberculosis (TB) when spontaneous sputum is smear negative.

However, there is a wide range in the diagnostic yield from bronchoscopy in suspected TB, this study was carried out to know the usefulness of bronchoscopy in sputum smear negative and CBNAAT negative patient of presumptive tuberculosis by direct visualization of bronchial tree and collecting specimen such as Bronchoalveolar lavage (BAL) and establish the diagnosis by examination of BAL for AFB by ZN stain, also BAL for solid and liquid culture and BAL for CBNAAT.

METHODS

It was a prospective observational study in the Department of Respiratory medicine at Dr. D.Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune for duration of 2 years (sept 2018 to Aug 2020) among 100 cases of presumptive tuberculosis whose sputum were negative on sputum AFB and CBNAAT. Study by Alzeer AH found that rate of bronchoscopy complication was 5%.[7]

Considering same proportion for this study using proportional sample size formula-n=4pq/l2 Where P=rate of complication (5%)q=100-p; 95,l=allowable error-5% of p; Calculated sample size using Open epi software was

73 at 95% confidence interval. For study purpose a total of 100 subjects were enrolled.

Inclusion criteria

Male and female patients above the age of 18 years with presumptive tuberculosis i.e an individual having cough for 2 weeks or more. Contacts of smear positive TB patients having cough for any duration. Suspected/confirmed extra pulmonary TB having cough for any durations. Sputum smear negatives, at least (2 attempts) and sputum for CBNAAT and those who gave informed consent for bronchoscopy.

Exclusion criteria

Relative or absolute contraindication for bronchoscopy were excluded from study.

Institute Ethics committee clearance was obtained before the start of study.

Details of study objective, risk of procedure, benefits and information about procedure was explained to patient in a language patient can understand and written informed consent was obtained.

At first visit patients of presumptive pulmonary tuberculosis was asked for sputum smear sample and sputum for CBNAAT. On second visit patients come with reports and decision for bronchoscopy was made depending on reports.

Complete evaluation of the patients was done in order to establish the diagnosis. All the patients of presumptive tuberculosis as per RNTCP guidelines who were sputum smear negative (2 attempts) and CBNAAT negatives (1 attempt) were selected for study.

Presumptive tuberculosis /tuberculosis suspect

An individual having cough for 2 weeks or more. Contacts of smear positive tb patients having cough for any duration. suspected /confirmed extra pulmonary tuberculosis having cough for any duration.

Screening Investigations for etiology and evaluating the risk of bronchoscopy like Sputum for AFB, gram stain, fungal stain, Sputum for mycobacterial culture, Sputum for gene expert, HIV test, hemogram with TLC, chest X ray and Electrocardiograph were carried out before enrollment.

All the presumptive pulmonary tuberculosis patients after screening for all the above investigation were subjected to bronchoscopy and 2-5ml of broncho alveolar fluid (BAL) was taken for ZN stain, mycobacterial and pyogenic culture, gene experts (CBNAAT) and malignancy to confirm diagnosis among study subjects. After bronchoscopy the patients who came positive for

MTB in BAL by ZN staining/ CBNAAT or solid/ liquid culture was advised for further management as per RNTCP protocol.

Post procedural monitoring was done for vitals, transient hypotension, hypoxia, bleeding, pneumothorax, bronchospasm, hypoxemia, epistaxis, nasal trauma, nausea and vomiting.

Data analysis

Data was entered in Microsoft word and analyzed using SPSS 20. Qualitative and quantitative data were expressed as frequency with percentage and mean+ SD with median and range. Descriptive statistics were used to summarize demographic and all other clinical characteristics of the participants. Frequency and percentages were computed for calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) using the standard formulae.

RESULTS

It was a cross sectional study among 100 sputum smear and CBNAAT negative suspected tuberculosis subjects attended to Tb chest department of a medical college. Maximum were in age group of 41-50yrs followed by 51-60 years. Mean age of study subjects was 47.31±12.29 years and range of 22-90 years. Among study subjects more than half were male. M:F was 1.2:1 and 5% had past history of tuberculosis.

Table 1: Baseline characteristics of study subjects.

Demographics	Frequency (n=100)	Percent
21-30 years	12	12
31-40 years	18	18
41-50 years	31	31
51-60 years	28	28
>60 years	11	11
Female	45	45
Male	55	55
Past h/o tuberculosis	5	5

Table 2: Diagnostic yield of BAL among study subjects.

BAL	Yield
Pyogenic culture sensitivity	24%
CBNAAT	14%
Solid/liquid culture	14%
Zn staining	10%
Malignancy	04%

Most common findings on chest X-ray among study subjects was alveolar opacities (40%), inhomogeneous opacity (24%), cavitary lesions (20%), cystic lesion (8%) and fibrosis (6%) in different zones of lung. Most commonly affected zone was right upper zone (39%) and

some of them having bilateral lower zone (24%) lung involvement. Right lung was affected in 39%, left lung in 35% and bilateral lung involvement was in 24% subjects. Only 2 subjects had normal findings on chest X ray.

Out of 100 BAL sent for CBNAAT testing 15% detected mycobacterial tb, 2% detected mycobacterial tb with Rif resistance. On Zn staining testing 10% showed AFB on microscopic findings, on culture 14% showed AFB growth,4% had malignant cell findings, culture sensitivity for ruling out microbiological cause of pneumonia testing 76% showed occasional pus cell, 21% showed gram positive cocci, and 3% showed klebsiela growth.

Table 3: Diagnostic accuracy of various methods on BAL Samples.

Methods	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
AFB stain	42.86	95.35	60	91.11
CBNAAT	78.85	93.02	64.71	96.39

Diagnostic efficacy of Zn staining of BAL showed 42.86% sensitivity, 95.35% specificity, 60% PPV, 91.11% NPV and 88% diagnostic accuracy. BAL CBNAAT testing had 78.57% sensitivity, 93.02% specificity, 64.71% PPV, 96.39% NPV and 91% diagnostic accuracy. Rate of complication was 10% and most common was bronchospasm and hypoxia.

DISCUSSION

Detecting patients with active Pulmonary Tuberculosis (PTB) disease is an important component of Tuberculosis (TB) control as early appropriate treatment renders these patients non-infectious and interrupts the chain of transmission of tuberculosis.[8] About 40 60% of patients with active pulmonary tuberculosis suspected clinically or radiologically may fail to produce sputum, or when it is available AFB/CBNAAT may be negative on repeated smear examination.[9]

Therefore more aggressive procedures need to be undertaken in these patients in order to establish early diagnosis and interrupt disease transmission. Fibreoptic bronchoscopy is considered as a safe diagnostic and interventional tool, for all age group including extremely premature infants and should be conducted on all patients without expectoration and negative sputum reports and that BAL performance should be a routine procedure as it is simple and usually uncomplicated technique.[10,11]

This prospective study was conducted to find diagnostic yield of bronchoscopy among sputum AFB & CBNAAT negative subjects. A total of 100 subjects were enrolled with mean age of 47.31±12.29 years and range of 22-90 yrs. M:F was 1.2:1. A study by Panda et al found majority were males (79.4%).[12] The mean age of the patients was 36.8 years. Other studies done by Iyer and by Shrestha et al had also found male predominance with

66.6% and 62.1% respectively.[13,14] In contrast to Khalil study shows female predominance (61.3%).[15]

Most common symptom in our study was cough followed by weight loss and fever. Panda found cough (66 %%) followed by loss of appetite (69.4%) and fever (54.4%) as main symptoms among study participants.[12] Cough was also chief presenting symptom in study done by Pierre (51.9%) Vivek 60%, Shrestha (71.7%), Sanjay (72.2%).[13,14,16,17]

In present study most common findings on chest X-ray among study subjects alveolar opacities (40%), inhomogeneous opacity (24%), cavitary lesions (20%), cystic lesion (8%) and fibrosis (6%) in different zones of lung. Most commonly affected zone was right upper zone (39%) and some of them having bilateral lower zone (24%) lung involvement.

Right lung was affected in 39%, left lung in 35% and bilateral lung involvement was in 24% subjects. Panda found consolidation (27.9%) followed by fibro cavitary diseases (23.5%).[90]

Similar study by Avashial reported on 74 patients the most common chest X ray finding was consolidation 24 (33.3%), fibrocavitary lesion 08 (11.1%),nodules 02 (2.8%),mass 02 (2.8%) interstitial shadows 02 (2.8%),thick walled cavity 2 (2.8%) bronchiectactic changes 05 (6.7%) other opacity 20 (27.8%) normal chest x-ray 7 (9.7%) respectively.[100]

Study conducted by, Khalil, Hazarika, Barnard also found that most common chest radiology abnormality was consolidation and fibrocavity lesion ranging 10-12% of patients. study by Chaudhary, right lung involvement was maximum i.e 83 (59.29%), followed by left sided involvement 35 (25%) and bilateral involvement 14 (10%) maximum were showing upper zone involvement 45 (32.14%) followed by equal involvement of lower zone and mid zone 28 (20%) and hilar involvement observed in 20 (14.29%).[15,18,19,20]

In our study on testing BAL to confirm tuberculosis diagnosis out of 100 presumptive patients, only 10% were BAL smear positive by ZN staining, 17% were detected by CBNAAT and 14% by Solid/liquid culture giving a total pulmonary tuberculosis diagnosis among 14%. Quaiser study showed BA smear was positive in 6 (15%) patients whereas when both BA smear and BA culture were combined, the positivity increased to 8 (20%) patients.[21]

Combining all the results of bronchoscopic procedures in Quaiser study, a definitive diagnosis of tuberculosis was possible in 17 (42.5%) of the 40 patients. In a study by Panda 12 out of 68 clinic-radiologically suspected patients, only 3 were BAL smear positive by ZN staining while another 29 were further detected by CBNAAT giving a total bacteriological figure of 32.

Similar study by Awashiya the yield by CBNAAT was 47.2% for smear-negative cases.[17] Study conducted by Hazarika concluded that Out of 162 patients 74 (45.67%) were BAL CBNAAT positive cases and the number of rifampicin sensitive cases were 65 (87.84%) and rifampicin resistant cases were 9 (12.16%) Kiluru study reported that out of 51 patients 31 (60.78%) patients were BAL Gene xpert mtb detected and 3 (9.6%) were rif resistance.[18,22]

Our results are little lower than earlier study, this could be due to different study design, inclusion exclusion criteria and geographic burden of tuberculosis. The diagnosis of pulmonary TB in patients with negative expectorated sputum results remains challenging due to variable diagnostic yields of any single test.[13]

In present study considering solid / liquid culture as a gold standard it was found that Zn staining had 42.86% sensitivity, 95.35% specificity, 60% PPV, 91.11% NPV and 88% diagnostic accuracy, CBNAAT testing had 78.57% sensitivity, 93.02% specificity, 64.71% PPV, 96.39% NPV and 91% diagnostic accuracy. Previous studies had sensitivity range of 80 to 95.7% and specificity of 91-100%.[15,16,23,24] Variation in findings of earlier study and present study may be due to difference in inclusion exclusion criteria of study participants, and diagnostic methods.

Flexible fiberoptic bronchoscopy with bronchial aspiration and bronchoalveolar lavage under local anaesthesia is a relatively safe procedure and well tolerated by most of the patients. Complications are known but rare in occurrence.[25-28] In our study most of the subjects (90%) didn't show any complication, rate of complication was 10% and most common was bronchospasm in 8 subjects and transient hypoxia was found in 2 subjects and there was no death.

Subjects with bronchospasm got recovered using simple measure like inhaler therapy and transient hypoxia subjects got recovered by using oxygen therapy. In Kalawat U study no complications occurred among patients undergoing bronchoscopy.[29] Also a study by Anderson and coworkers didn't report any complications. Fiberoptic bronchoscopy is useful in establishing accurate and early diagnosis of lower respiratory tract infection.[30]

CONCLUSION

Bronchoscopy reveals a higher bacteriological confirmation of diagnosis in patients with strong clinical and radiological evidence suggestive of pulmonary tuberculosis with minimal rate of complication during procedure. Flexible fiberoptic bronchoscopy will be a helpful additional tool in diagnosis of sputum negative and clinically suspected tuberculosis patient which helps to early detection and interrupt disease transmission. This procedure is relatively safe and sound.

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