

Diagnostic utility of chest computerized tomography in the diagnosis of recurrence among sputum scarce and sputum negative previously treated pulmonary tuberculosis suspects

BG Bharath¹, Animesh Ray¹, Pankaj Jorwal¹, Surabhi Vyas², Manish Soneja¹, Ashutosh Biswas¹, Sanjeev Sinha¹, Maroof A Khan³

¹Department of Medicine, All India Institute of Medical Sciences, New Delhi, India, ²Department of Radiology, All India Institute of Medical Sciences, New Delhi, India, ³Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India

ABSTRACT

Objective: The objective was to study the sensitivity, specificity, and diagnostic accuracy of various computed tomography (CT) chest findings in diagnosing recurrence among pulmonary tuberculosis (PTB) suspects. **Materials and Methods:** A prospective observational study was conducted in a tertiary care hospital in New Delhi. A total of 130 suspects with a past history of treatment for PTB, who presented with any of the symptoms suggestive of recurrence were included. Sputum-positive, HIV-positive patients, pregnant females, and patients aged <18 years were excluded. Patients underwent CT chest followed by bronchoalveolar lavage (BAL). **Results:** A total of 62 patients were there in the final analysis. The median age of the patients with recurrent PTB was 27.5 years. Cough was the universal symptom in all these patients (>90%). Hemoptysis was the predominant symptom among patients with chronic pulmonary aspergillosis (66.6%). Necrotic mediastinal lymph nodes had good diagnostic accuracy of 88.71% with area under the curve of 0.806, $P < 0.001$ in diagnosing recurrent TB. BAL GeneXpert and mycobacteria growth indicator tube had good sensitivity (83.33% and 84.62%, respectively), specificity (100% for both), and excellent diagnostic accuracy (95.16% and 96.36%, respectively) for diagnosing recurrence in sputum negative and sputum scarce patient, ($P < 0.001$) when compared with composite reference standard. For culture-positive cases, BAL GeneXpert MTB/RIF had 100% sensitivity and 97.73% specificity in diagnosing recurrent PTB patients. **Conclusion:** The presence of mediastinal necrotic lymph node is the most accurate CT finding that can differentiate recurrent TB from post-TB sequelae. No other single chest CT scan finding had reliable diagnostic accuracy in comparison to microbiological tools in diagnosing recurrence among sputum negative or scarce previously treated PTB suspects.

KEY WORDS: Bronchoalveolar lavage GeneXpert, composite reference standard, sputum scarce

Address for correspondence: Dr. Pankaj Jorwal, Department of Medicine, All India Institute of Medical Sciences, New Delhi, India.

E-mail: pankajjorwal.aiims@gmail.com

Submitted: 13-Feb-2021

Revised: 21-Feb-2021

Accepted: 24-Feb-2021

Published: 28-Feb-2022

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

Access this article online	
Quick Response Code: 	Website: www.lungindia.com
	DOI: 10.4103/lungindia.lungindia_103_21

How to cite this article: Bharath BG, Ray A, Jorwal P, Vyas S, Soneja M, Biswas A, *et al.* Diagnostic utility of chest computerized tomography in the diagnosis of recurrence among sputum scarce and sputum negative previously treated pulmonary tuberculosis suspects. Lung India 2022;39:145-51.

INTRODUCTION

Tuberculosis (TB) is considered a global threat with high incidences in developing countries. According to WHO Global TB Report in the year 2018, about 6.7 million cases of TB were reported across the world and 18% of these were drug-resistant cases. There were 6.4 million new or relapse cases, of which 86% were pulmonary, 0.92 million (14.38%) cases were HIV positive and 0.558 million (3.5%) cases were drug-resistant TB patients.^[1] In India, 19 lakh total cases were notified in 2018, among which 17.9 lakh were new or relapse cases. Pulmonary TB (PTB) accounted for 85% of new or relapse cases and 7.1% cases were drug resistant. Total mortality due to TB was 4.1 lakh cases in TB patients without HIV and 11,000 in patients with HIV and TB—indicating that the disease is a “major” killer in India.^[1]

In a patient with newly suspected PTB, sputum smear microscopy, culture, and chest x-ray (CXR) are the initial investigations performed. Computed tomography (CT) chest may be needed subsequently to confirm lesions on x-ray or detect new lesions, for evaluation of mediastinal lymph nodes, assessing disease activity, or for evaluating complications. Bronchoalveolar lavage (BAL) is helpful in diagnosis in sputum negative or scarce patients and can identify TB in 41% of patients who are sputum negative or scarce.^[2]

When a patient, previously cured of TB is afflicted by TB again, it is labeled as recurrence. 2-year incidence rate of recurrence after treatment of PTB with rifampicin-containing regimens ranges from 0% to 27%.^[2,3] A study conducted in India, across 6 states by Velayutham *et al.*^[4] showed the pooled TB recurrence estimate was 10.9% over 1-year follow-up and TB recurrence rate per 100 people-years was 12.7%. As sputum examination is positive in up to 95% of these patients, sputum examination remains the first choice in diagnosing recurrence of PTB in patients presenting with expectoration. Sputum negative and scarce patients pose a significant diagnostic dilemma. In this sub-group of patients, diagnosis is often based on clinical, radiological, Broncho-alveolar fluid examination or therapeutic trial with anti-tubercular therapy. Due to the persistence of residual radiological lesions both X-ray and CT have limitations in detecting disease activity.^[5]

This study was thus designed to assess the usefulness of CT chest and compare it with yield of BAL as well as composite reference standard (CRS) in diagnosis of recurrence among patients with suspected PTB who were sputum negative and sputum scarce. This study tried to identify the factors (clinical and radiological) which could predict the presence of recurrence of active TB.

MATERIALS AND METHODS

Subjects and population

This was a prospective observational study conducted at a tertiary care hospital in India, between July 2017 and April

2019. Patients who were more than 18 years of age were having a history of PTB treated in past and now presented with any one or more of the following symptoms like cough duration of >3 weeks with or without hemoptysis, prolonged fever with or without history of evening rise of temperature or night sweat, significant weight loss or loss of appetite were included in the study. All those patients who refused to give consent or were sputum positive, had extrapulmonary involvement, pregnancy, and HIV positivity were excluded.

Specimen processing

All selected samples were subjected to the routine diagnostic test of acid-fast bacilli (AFB) stain smear, Gene Xpert® MTB/RIF assay. The samples were processed using the NALC-NaOH decontamination procedure (final NaOH concentration, 1%). The decontaminated and digested samples were put in mycobacteria growth indicator tube (MGIT) culture for the confirmation of *Mycobacterium tuberculosis*.

Data collection

Patients who fulfilled inclusion and exclusion criteria were recruited from the OPD and wards of the teaching hospital.

Definitions

CRS: A CRS is a fixed rule used to make a final diagnosis based on the results of two or more tests, referred to as component tests. For each possible pattern of component test results (test profiles), a decision is made about whether it reflects the presence or absence of the target disease.^[6] The diseases were defined as follows. Recurrent PTB: Based on the clinical presentation (symptoms as per inclusion criteria), radiological and/or BAL findings, and final response to anti-tubercular treatment. Post-TB sequelae with secondary infection: Based on clinical presentation, radiological and BAL findings along with response to a course of oral or intravenous antibiotics. Post-TB sequelae with chronic pulmonary aspergillosis: CT showing aspergilloma, elevated BAL galactomannan, raised serum *Aspergillus* specific IgG and/or positive precipitin test, and response to therapy. Post-TB sequelae with obstructive airway disease (OAD): Based on clinical presentation, CT findings and pulmonary function tests, and response to symptomatic treatment.

Statistical analysis

Data were recorded in a pre-designed proforma. Continuous variables were summarized as mean and standard deviation or median and range (for nonparametric data). Quantitative variables were analyzed using parametric (Student's *t*-test) or nonparametric tests (Kruskal-Wallis test), as applicable. All qualitative variables were summarized as frequency (percentage) and were analyzed with Chi-square or Fischer's exact test. The statistical analysis was performed using IBM, Windows, Version 25.0. Armonk, New York: IBM Corporation. A *p*-value of <0.05 was considered as statistically significant.

RESULTS

A total of 130 patients who had history of treated PTB and presented to medicine OPD or were admitted in medicine ward with any of the following symptoms suggestive of recurrence like, cough of >3 weeks with or without associated hemoptysis, prolonged fever with or without a history of evening rise in temperature or night sweat, significant weight loss (>5% weight loss over 6 months to 1 year) or loss of appetite were screened.

After excluding sputum-positive, HIV-positive patients and patients aged <18 years, 87 patients were included in the

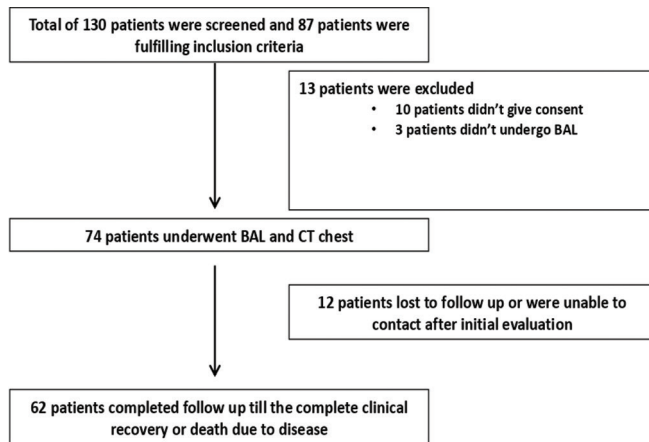


Figure 1: Flow chart showing screened and included patients

study. Among those 87 patients, 10 patients did not give consent, 3 patients did not undergo for sampling while 12 patients do not come for follow-up after giving consent for bronchoscopy. After excluding these 25 patients, the remaining 62 patients who underwent both BAL and CT chest were included in the study. CT findings were divided into active, indeterminate, and healed groups [Table 1].^[5] BAL samples were sent for AFB stain, GeneXpert and MGIT culture, gram stain, KOH, bacterial and fungal culture. A detailed flow chart depicting the flow of patient follow-up is shown in Figure 1.

Final diagnosis

Recurrent PTB was present in 18 of 62 (29%) patients. Among others, 16 (26.8%) had post-TB sequelae with secondary bacterial infection, 15 (24.2%) had chronic pulmonary aspergillosis, and the remaining 13 (21.0%) had post-TB sequelae with OAD. One among 18 patients with recurrent PTB was a case of multidrug-resistant TB.

Baseline characteristics and symptomatology

The median age of the patient cohort was 33 years. Out of 62 patients, 39 patients were male (62.9%) and 23 were females (37.1%). The baseline characteristics of patients with recurrent TB as compared with other diagnoses are shown in Table 2.

About 72.2% of the patient among the recurrent PTB group developed symptoms within 2 years. The median interval between two episodes of PTB was 1.5 years

Table 1: Indicators of congenital tuberculosis disease activity on chest x-ray and computed tomography

Features of active TB	Features indeterminate for TB	Features of healed TB
Air-space nodules/centrilobular nodules/clustered nodules in apical and posterior segments RUL, apicoposterior segment LUL, RML, lingula, superior segment any LL	Consolidation/centrilobular nodules in other segments	Thin-walled cavity
Consolidation in above mentioned regions with ipsilateral LN enlargement	Ground glass opacities: May suggest superimposed secondary infections or aspiration related	Bronchiectasis±bronchial wall thickening
Miliary nodules	Cavity with air-fluid level: Usually indicates secondary infection	Fibroparenchymal opacities
Cavity with surrounding consolidation	Borderline enlarged discrete LNs with homogeneous enhancement or preserved perinodal fat	Thick-walled cavity atelectasis/collapse
Enlarged mediastinal LNs with central necrosis (rim enhancement) or heterogeneous enhancement		Well defined small nodules±calcification
Conglomeration of LNs or obscuration of perinodal fat pleural thickening/calcification		Subcentimetric LNs±calcification
Effusion/empyema with split pleura sign		

TB: Tuberculosis, LUL: Left upper lobe, RUL: Right upper lobe, RML: Right middle lobe, LL: Lower lobe, LN: Lymphadenopathy

Table 2: Comparison of demographic details between recurrent tuberculosis and other causes

	Recurrent TB	Other causes	P
Age, years (median±SD)	27.5±13.9	35.0±11.3	0.295
Gender, n (%)			
Male, n=38	10	29	0.413
Female, n=22	8	15	
Weight at presentation (kg±SD)	42.39±9.57	49.00±9.26	0.015
Weigh at the end of follow-up (kg±SD)	49.80±9.98	51.44±8.59	0.545
Duration from last episode of TB (years±SD)	2.98±3.85	6.24±7.0	0.069
Hb, g/dL (mean±SD)	10.95±1.69	12.45±2.42	0.061
Albumin (mean±SD)	4.18±0.38	4.49±0.49	0.051
ESR, mm/h (mean±SD)	39.31±8.36	31.44±15.13	0.091
CRP, mg/dL (mean±SD)	83.03±79.02	11.76±24.41	0.037

TB: Tuberculosis, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, Hb: Hemoglobin, SD: Standard deviation

and ranged between 1 and 15 years. Patients with other etiologies usually presented later with a medial interval of 4 years with a range between 1 and 37 years. There was a statistically significant difference in interval between the previous episode of PTB and current ailment (recurrent TB vs. others) between the two groups, ($P = 0.029$).

Cough was the most common symptom in both recurrent PTB and other etiologies (>90% in both groups). Fever was present in 72.2% of patients with recurrent PTB and 68.7% of patients with secondary bacterial infection. Weight loss was significantly more in recurrent PTB patients compared to other etiologies, ($P < 0.001$). Hemoptysis was significantly higher in patients with pulmonary aspergillosis (66.6%) compared to recurrent PTB (11%), ($P < 0.001$).

A total of 18 patients were diagnosed with recurrent PTB using CRS. Among these 18 patients, 15 were BAL GeneXpert positive (6 were AFB positive and MGIT culture positive was 11 patients). BAL AFB was positive in one of the remaining 44 patients in whom BAL GeneXpert and MGIT culture were found negative. He was later diagnosed to have post-TB sequelae. One of the 18 patients with recurrent PTB had BAL GeneXpert positive but MGIT was negative.

Sensitivity and specificity for BAL GeneXpert, MGIT culture and AFB was 83.33%, 84.62%, 33.33% and 100%, 100%, 97.73%, respectively [Table 3]. BAL GeneXpert had 100% sensitivity and 97.73% specificity for culture positive cases, $P < 0.001$.

GeneXpert and MGIT culture had excellent diagnostic accuracy (area under the curve [AUC] of 0.962 and 0.923, respectively, $P < 0.001$), whereas AFB had poor diagnostic accuracy (AUC = 0.680).

Computed tomography chest findings

Various CT findings were divided into findings suggestive of active, indeterminate, and healed TB [Table 1]. CT

findings suggestive of active TB like air space nodules, tree in bud configuration [Figure 2], consolidation, thick-walled cavity, cavity with surrounding consolidation [Figure 3], and necrotic mediastinal lymph nodes [Figure 4] were compared between recurrent PTB and other etiologies.

Air space nodules were present in 88.8%, 87.5%, 60%, and 92.3% in patients with recurrent PTB, secondary bacterial infection, chronic pulmonary aspergillosis, and OAD, respectively. Tree in bud configuration though was more frequent in patient with recurrent PTB and secondary bacterial infection (61.1% and 43.4%, respectively) but was also seen in patient with pulmonary aspergillosis and OAD (in 20% and 23%, respectively). Air space nodules were present in all four groups (more than 60% of cases in each group) and had poor specificity. Tree in bud configuration significantly differentiated recurrent PTB from pulmonary aspergillosis and OAD, $P = 0.017$ and 0.036, respectively. However, it could not differentiate between recurrent PTB from secondary bacterial infection. Sensitivity, specificity, positive predictive value (PPV), and negative productive value (NPV) of air space nodules and tree in bud configuration for differentiating recurrent PTB from other etiologies are elaborated in Table 4. Both air space nodules and tree in bud configuration had poor diagnostic accuracy (0.547 and 0.658, $P = 0.566$ and 0.078, respectively).

Among pulmonary aspergillosis patients, about 53% (8/15) had thick-walled cavities and about 33% of these had cavities with surrounding consolidation. Both of these CT features were also present in patients with secondary bacterial infection and recurrent PTB, however in lesser frequency. None of the patients with OAD had these CT findings. Sensitivity, specificity, PPV, and NPV of thick-walled cavity and cavity with surrounding consolidation are elaborated in Table 4.

Consolidation was present in 50% of recurrent PTB patients. Among patients with chronic pulmonary aspergillosis, secondary bacterial infection, and post-TB sequelae with OAD, consolidation was present in

Table 3: Various microbiological parameters

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	P
BAL Gene Xpert	83.33 (58.58-96.42)	100 (91.96-100.0)	100.0	93.62 (83.92-97.63)	95.16 (86.50-98.99)	<0.001
BAL MGIT culture	84.62 (54.55-98.08)	100.0 (91.59-100.0)	100.0	95.45 (85.44-98.69)	96.36 (87.47-99.56)	<0.001
BAL	33.33 (13.34-59.01)	97.73 (87.98-99.94)	85.71 (43.71-97.89)	78.81 (72.04-83.29)	79.03 (66.82-88.34)	<0.001

PPV: Positive predictive value. NPV: Negative predictive value, BAL: Bronchoalveolar lavage, MGIT: Mycobacteria growth indicator tube

Table 4: Recurrent tuberculosis versus others etiologies

	Sensitivity	Specificity	PPV	NPV	Accuracy	P
Air space nodules	88.89 (65.29-98.62)	20.45 (9.80-35.30)	31.37 (26.81-36.33)	81.82 (51.83-94.95)	40.32 (928.05-53.55)	0.382
Tree in bud pattern	61.11 (35.75-82.70)	70.45 (54.80-83.24)	45.83 (32.00-60.34)	81.58 (70.64-89.07)	67.74 (54.66-79.06)	0.021
Consolidation	50.00 (26.02-73.98)	77.27 (62.16-88.53)	47.37 (30.58-64.77)	79.07 (69.85-86.03)	69.35 (56.35-80.44)	0.034
Thick walled cavity	33.33 (13.34-59.01)	79.55 (64.70-90.20)	40.00 (21.74-61.54)	74.47 (67.06-80.69)	66.13 (52.99-77.67)	0.334
Cavity with surrounding consolidation	22.22 (6.41-47.64)	86.36 (72.65-94.83)	40.00 (17.57-67.58)	73.08 (67.37-78.11)	67.74 (54.66-79.06)	0.457
Necrotic mediastinal LN	61.11 (35.75-82.70)	100.00 (91.96-100.00)	100.00	86.27 (77.89-91.81)	88.71 (78.11-95.34)	<0.001
Homogenous mediastinal LN	11.11 (1.38-34.71)	68.18 (52.42-81.39)	12.50 (3.48-36.13)	65.22 (59.12-70.85)	51.61 (38.56-64.50)	0.091

PPV: Positive predictive value, NPV: Negative predictive value, LN: Lymphadenopathy

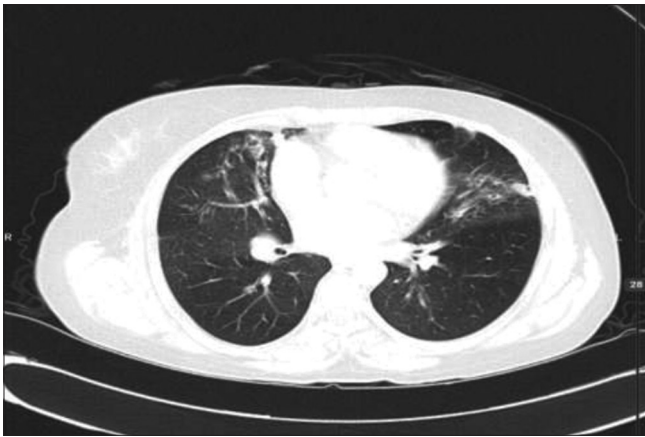


Figure 2: Centrilobular tree in bud nodules seen in lingula, anterior segment right middle lobe



Figure 3: Cavity with surrounding consolidation in the superior segment of left lower lobe

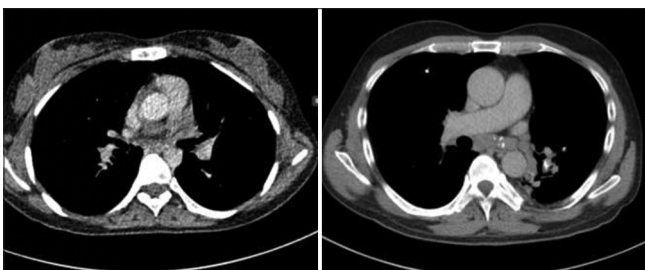


Figure 4: CT chest showing presence of necrotic mediastinal lymph nodes

53.3%, 12.5%, and 0% of the patients, respectively. The presence of consolidation could not differentiate between recurrent PTB and other etiologies except OAD. AUC for consolidation was 0.636, ($p = 0.094$) in differentiating recurrent PTB from other etiologies. Consolidation had overall specificity of 77.27% and sensitivity of 50.0% in differentiating recurrent PTB from other etiologies. The frequency of occurrence of homogenous lymph nodes in recurrent PTB, secondary bacterial infection, pulmonary aspergillosis, and OAD was 11%, 43.7%, 40%, and 23%, respectively. However, necrotic mediastinal lymph nodes were present only in patients with recurrent PTB patients.

Necrotic mediastinal lymph nodes had good diagnostic accuracy of 88.71% with AUC of 0.806, $P < 0.001$. Overall sensitivity, specificity, PPV and NPV of necrotic mediastinal lymph nodes for differentiating patients with recurrent PTB from other etiologies was 61.11%, 100.0%, 100% and 86.27%, respectively, $P < 0.001$.

The final CT diagnosis was made by an expert radiologist who was blinded from microbiological reports but not from the clinical details of the patient. Findings were grouped into active, indeterminate, and healed TB based, and final CT diagnosis of active recurrent TB was made based on the radiologist's opinion. If CT findings were of indeterminate or of healed TB then, the final CT diagnosis was made as "aetiology other than recurrent PTB". Final CT diagnosis had diagnostic accuracy of 80.65%, AUC 0.804, $P = 0.001$, compared to diagnostic accuracy of 96.36% for BAL MGIT with AUC of 0.923, $P < 0.001$.

Multivariate logistic regression between various computed tomography findings

Among the various CT findings that were discussed previously, tree in bud [Figure 2] configuration ($P = 0.021$), consolidation (0.034) [Figure 3], enlarged necrotic (<0.001) mediastinal lymph nodes [Figure 4] were statistically significant in differentiating recurrent PTB from other etiologies. All the above CT findings were included for multivariate linear regression. On multivariate regression, the presence of necrotic mediastinal lymph node was the single most CT finding which could significantly differentiate between recurrent PTB and other etiologies.

DISCUSSION

This study included sputum negative or scarce patients with a past history of PTB and having recurrent chest symptoms. Patients with a past history of PTB presenting with recurrent chest symptoms like prolonged cough (>2 weeks), fever, hemoptysis, dyspnea, and constitutive symptoms like weight loss, appetite can have multiple differential diagnoses. Besides, recurrence of PTB, other potential causes can be pulmonary aspergillosis, post-TB bronchiectasis with a secondary bacterial infection, post-TB sequelae with OAD, nontuberculous mycobacteria (NTM) infections, etc., The diagnostic modalities commonly employed usually include a CT chest as CXR often is not sensitive enough to differentiate between new and residual changes. Microbiological confirmation is important but may be negative in a sizeable proportion of cases often requiring empirical of anti-TB treatment based on clinicroadiological parameters. This study endeavored to measure the diagnostic yield of CT chest features in confirmation with microbiological results and CRS.

In this study, the percentage of recurrence among the study group was high (29%) compared to previous studies.^[4] This is because this study categorically included patients with suspicion of recurrence (symptomatic patients).

In the study there was no gender difference in the occurrence of recurrent PTB and most subjects belonged to the young age group (mean age = 31.17 years), similar to other studies from India.^[4] The median age of patients with recurrent PTB was 27.5 years and that of patients with other diagnoses was 35 years. There was however no significant difference between the two groups, $P = 0.353$. Most of the patients with a history of PTB had recurrent episodes within 2 years.^[7] The median duration between the 2 episodes in the current study was 1.5 years. In a recent study reported from India,^[4] the recurrence rate of PTB in 1 year was 10.9%. Several studies showed that up to 72% of patients who had recurrence, had previous TB within the last 1–3 years.^[8]

Cough was the most common symptom complained by the patients (93.5%). The presence of cough for more than 2 weeks is included in the WHO definition of PTB suspects. However, in patients who already had a previous episode of PTB, prolonged cough can occur due to etiologies other than recurrent PTB like pulmonary aspergillosis, post-TB bronchiectasis with secondary infection, OAD, or other causes like NTM infection, etc. In this study, fever was present in up to 72.2% of patients with recurrent PTB but it was significantly associated with recurrence of TB as compared with other etiologies of exacerbated chest symptoms in the study population. In this study maximum number of cases of hemoptysis was present in pulmonary aspergillosis (66.6%) followed by post-TB bronchiectasis with secondary infection (43.7%). Hemoptysis was also seen in 11% of recurrent PTB patients.

However, none of the symptoms statistically predicted the recurrence over and above the other differentials except significant weight loss. In our study, 94.4% of patients with recurrent PTB had a history of weight loss at presentation.

Bronchoscopy is a useful procedure in the evaluation of patients with sputum negative PTB. The diagnosis rate using bronchoscopy is as high as 86.6% with minimal risk of complications in experienced hands.^[9]

A previous study from All India Institute of Medical Sciences, New Delhi conducted in 60 patients showed that BAL GeneXpert had a sensitivity and specificity of 81% and 73% in culture-confirmed cases; 46% and 100% for the final diagnosis; 32% and 100% in culture-negative cases, respectively. BAL culture had a sensitivity of 32% for the final diagnosis.

In our study, BAL GeneXpert was positive in 15 out of 18 patients with recurrent PTB diagnosed based on CRS and hence had sensitivity of 83.33% and specificity of 100.0% for the diagnosis of sputum negative PTB in patient with a past history of TB. BAL culture (MGIT) was positive in 11 patients out of 13 patients in the recurrent PTB group. BAL culture (MGIT) had 84.76% sensitivity and 100.0% specificity. When compared to culture-positive cases

GeneXpert had 100.0% sensitivity and 97.73% specificity in diagnosing recurrent PTB.

BAL GeneXpert and MGIT had excellent diagnostic accuracy (95.16% and 96.6%, respectively) in diagnosing recurrent PTB, which is almost similar to previous studies^[4,10] which were done in sputum negative and scarce patients.

The presence of necrotic mediastinal lymph nodes was the single CT finding which significantly helped in differentiating between recurrent PTB and other etiologies. It had very good diagnostic accuracy (88.71%), 61.1% sensitivity, and 100.0% specificity. However, non-necrotic lymph nodes did not differentiate recurrent PTB from other etiologies. Air space nodules are often considered to represent active infection especially when present in apical and posterior segments right upper lobe, apicoposterior segment left upper lobe, right middle lobe, lingula, superior segment any lower lobe.^[5] However, the presence of this finding in our study did not differentiate between recurrent TB and other etiologies. Air space nodules were seen in more than 80% of patients with secondary bacterial infection and OAD apart from recurrent PTB patients. The presence of tree in bud configuration, consolidation, and thick-walled cavity are considered signs of active infection and bronchial spread. However, secondary bacterial infection and pulmonary aspergillosis can also lead to the above CT findings and hence can mimic active PTB.

Other CT findings which are suggestive of active infection noted in a previous study^[5] did not significantly differentiate between recurrent PTB and sequelae in our patient cohort.

These include:

1. Pleural effusion (3 patients; 2 had post-TB sequelae and 1 had recurrent PTB)
2. Ground glass opacity (3 patients with aspergillosis and active hemoptysis)
3. Conglomeration of lymph nodes (1 patient with pulmonary aspergillosis)
4. Cavity with air-filled level (1 patient with secondary infection).

This is due to the occurrence of these findings in other etiologies as shown above.

While making the final CT diagnosis by a radiologist, the presence of only centrilobular nodules irrespective of its location, isolated consolidation, or thick-walled cavity without surrounding consolidation were considered indeterminate for diagnosis. Final CT diagnosis had a diagnostic accuracy of 80.65% considering indeterminate for PTB as non TB. However, when indeterminate TB was considered as active TB its diagnostic accuracy was reduced to 67.74%.

The presence of aspergilloma and high attenuation mucus fairly helped in making diagnosis other than recurrent PTB

CONCLUSION

The presence of mediastinal necrotic lymph node is the most accurate CT finding that can differentiate recurrent TB from post-TB sequelae. Other findings like tree in bud appearance and consolidation could only differentiate active infection from post-TB sequelae but not between active TB, pulmonary aspergillosis, and secondary bacterial infection.

Acknowledgment

The authors would like to acknowledge the Department of Medicine at AIIMS, New Delhi for their incessant support during the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. WHO | Global Tuberculosis Report 2018. WHO; 2018. Available from: http://www.who.int/tb/publications/global_report/en/. [Last cited on 2018 Nov 03].
2. Lambert ML, Hasker E, Van Deun A, Roberfroid D, Boelaert M, Van der Stuyft P. Recurrence in tuberculosis: Relapse or reinfection? *Lancet Infect Dis* 2003;3:282-7.
3. Gonzalez-Montaner LJ, Natal S, Yongchaiyud P, Olliaro P. Rifabutin for the treatment of newly-diagnosed pulmonary tuberculosis: A multinational, randomized, comparative study versus Rifampicin. Rifabutin Study Group. *Tuber Lung Dis* 1994;75:341-7.
4. Velayutham B, Chadha VK, Singla N, Narang P, Gangadhar Rao V, Nair S, *et al.* Recurrence of tuberculosis among newly diagnosed sputum positive pulmonary tuberculosis patients treated under the Revised National Tuberculosis Control Programme, India: A multi-centric prospective study. *PLoS One* 2018;13:e0200150.
5. Bhalla AS, Goyal A, Guleria R, Gupta AK. Chest tuberculosis: Radiological review and imaging recommendations. *Indian J Radiol Imaging* 2015;25:213-25. doi: 10.4103/0971-3026.161431.
6. Naaktgeboren CA, Bertens LC, van Smeden M, de Groot JA, Moons KG, Reitsma JB. Value of composite reference standards in diagnostic research. *BMJ* 2013;347:f5605.
7. Rate of reinfection tuberculosis after successful treatment is higher than rate of new tuberculosis | *American Journal of Respiratory and Critical Care Medicine*. Available from: <https://www.atsjournals.org/doi/full/10.1164/rccm.200409-1200OC>. [Last accessed on 2019 Jun 21].
8. Akpabio US, de Villiers PJ. Description of patients with recurrence of Pulmonary Tuberculosis in a Tuberculosis Hospital, Ermelo. *Afr J Prim Health Care Fam Med* 2011;3:261
9. Kalawat U, Sharma KK, Reddy PN, Kumar AG. Study of bronchoalveolar lavage in clinically and radiologically suspected cases of pulmonary tuberculosis. *Lung India* 2010;27:122-4.
10. Shin JA, Chang YS, Kim TH, Kim HJ, Ahn CM, Byun MK. Fiberoptic bronchoscopy for the rapid diagnosis of smear-negative pulmonary tuberculosis. *BMC Infect Dis* 2012;12:141.