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Radio-Diagnosis

SIGNIFICANCE OF HIGH-RESOLUTION COMPUTED TOMOGRAPHY CHEST FINDINGS IN DIAGNOSING SUSPECTED SPUTUM SMEAR-NEGATIVE ACTIVE PULMONARY TUBERCULOSIS

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ABSTRACT **Background:** Tuberculosis is one of the most common infectious diseases worldwide. With a high proportion of pulmonary tuberculosis (PTB) cases being sputum smear negative along with poor sensitivity of sputum smear examination for acid fast bacilli (AFB), the need for rapid and accurate diagnosis of smear negative PTB becomes an absolute essential for disease management. **Aims:** To describe the findings of high-resolution computed tomography (HRCT) in sputum smear- negative pulmonary tuberculosis (PTB), to determine the utility of HRCT in the diagnosis of PTB and to define the role of HRCT in predicting the risk of sputum smear-negative PTB among suspected PTB patients. **Methods:** 70 patients with suspected pulmonary TB having negative sputum smears for acid-fast bacilli were included and were subjected to HRCT chest. Patients were categorized in two groups based on the final diagnosis as PTB and non-PTB (non-pulmonary tuberculosis). Comparison of clinical features, laboratory parameters, chest x-ray and HRCT-findings of both PTB and non-PTB patients was done using the chi-square test. Provisional HRCT diagnostic criteria were designed to rank the risk of smear negative PTB among suspected PTB patients. **Results:** A positive Mantoux test alone is associated with a significantly increased risk of smear - negative PTB among suspected PTB patients. The Chi square test showed that the presence of centrilobular nodules, large nodules, tree-in-bud appearance, lobular consolidation, and the main lesion being located in S1, S2, and S6 were associated with an increased risk of smear negative PTB among suspected PTB patients. Ranking of the results using our HRCT diagnostic criteria provided good (Sensitivity 62.96% and Specificity 93.75%, with Rank 3 criteria) results for predicting PTB risk among suspected PTB patients. **Conclusions:** HRCT can predict the risk of PTB with good reproducibility, even in the setting of negative sputum smears, and can accurately select patients with a high probability of PTB among suspected PTB patients.

KEYWORDS : pulmonary tuberculosis, high-resolution computed tomography, sputum smear-negative, centrilobular nodules, large nodules, tree-in-bud appearance, lobular consolidation

INTRODUCTION:

Tuberculosis (TB) is a global health problem and the leading cause of death due to infectious diseases exceeding those caused by acquired immunodeficiency syndrome (AIDS). A total of 1.4 million people died of tuberculosis in 2019 worldwide. Usually, half to one-third of pulmonary tuberculosis (PTB) cases are smear-negative. There is a direct correlation between smear positivity and infectivity, but smear-negative also transmits the infection. Early diagnosis is essential in both cases for early institution of treatment and prevention of infection. The diagnosis of a patient with smear-negative PTB is difficult and often delayed, which results in the continuous spread of tuberculosis within the community.

The sensitivity of sputum smear examination for acid-fast bacilli is poor. The polymerase chain reaction (PCR) can rapidly diagnose PTB, but its sensitivity is low. Culture for mycobacterium tuberculosis is a slow method that takes 4-8 weeks. Bronchoscopy has been regarded as an effective alternative method. However, it is an invasive procedure that needs expertise. A high probability of PTB needs to be identified among smear-negative findings without missing patients who have PTB. Therefore, in smear-negative patients, the diagnosis of PTB can be made based on clinical features, radiological findings, and laboratory tests. A decision to treat or not to treat a smear-negative patient based on radiographic findings compatible with TB is a critical issue in saving an inactive patient from potential risks of anti-tuberculous drugs or in avoiding progression or transmission of the disease that results from withholding treatment in patients with active disease.

The chest radiograph (CXR) as a tool for diagnosing active PTB is sensitive but has poor specificity. High-resolution computed tomography (HRCT) is usually recommended when the chest radiograph is normal or inconclusive, but PTB is suspected clinically. Available data has shown a relationship between morphologic findings on HRCT and the number of AFB on sputum smears in patients with PTB.

In this study, we describe the HRCT chest findings in sputum smear-negative PTB and evaluate its role in predicting the risk of sputum smear-negative PTB among suspected PTB patients.

MATERIALS AND METHODS:

This study included 70 adult patients of either sex who presented to our department, where the study was conducted between January 2015 to May 2016. All patients with clinical suspicion of PTB were sputum smear-negative for acid-fast bacilli (AFB) on at least two different occasions or who did not expectorate sputum and old tuberculosis cases with suspected tuberculosis reactivation were included in the study. The sputum smear-positive AFB patients, pregnant patients, patients less than 18 years of age, and patients with contraindications to contrast-enhanced computed tomography (CECT) examination were excluded.

The procedure was explained to the patient, and written informed consent was obtained in every case in the vernacular language.

Relevant demographic and clinical details and laboratory parameters such as total leucocyte count (TLC), erythrocyte sedimentation rate

(ESR), and Mantoux test were recorded. Chest radiographs (CXR) were obtained for all the patients.

The high resolution computed tomography (HRCT) of the chest was done in all patients. The patients were imaged on a 128 slice multidetector computed tomography (MDCT) scanner set to 0.6 mm collimation and a pitch of 1.5 after overnight fasting. The CECT scan of the chest was acquired 55-60 seconds after intravenous administration of non-ionic iodinated contrast (300mgI/ml) at a dose of 1ml/kg, with the patient in a supine position during a single breath-hold. All CT images were evaluated in the lung (W:1500 L:-500) and mediastinal (W:500 L:50) window level settings. For HRCT sections, the images were reconstructed with a 1-mm slice thickness in the axial plane using a high spatial frequency bone algorithm. Sagittal and coronal reconstructions were also obtained.

The following HRCT chest findings were investigated: nodules [centrilobular nodules (< 8mm), clustered nodules, miliary nodules, calcified nodules, large nodules (> 8 mm), mass (> 20 mm), tree-in-bud pattern], lobular consolidation, interlobular septal thickening, ground-glass opacity, calcified lesions, fibrotic lesions, cavity, bronchial changes (bronchial wall thickening, bronchiectasis), Pleura (pleural effusion, pleural thickening), lymph nodes (mediastinal lymphadenopathy, lymphadenopathy at other sites).

Statistical analysis:
All statistical analyses were performed using SPSS software. Each of the HRCT findings found in patients of sputum smear-negative PTB were expressed in percentages. The various HRCT findings with the clinical and laboratory findings were studied using Pearson's chi-square test and Fisher's exact test. The unpaired 't's test analyzed the mean values of categorical data. The sensitivity, specificity, and diagnostic accuracy of HRCT chest in predicting disease activity were also calculated.

Based on the results obtained, the diagnostic criteria for diagnosing sputum smear-negative PTB among suspected PTB was designed by assigning a ranking to a combination of HRCT findings.

RESULTS:
A total of 70 patients with suspected pulmonary tuberculosis (PTB)whose sputum smear was negative were evaluated. Out of the 70 patients, 60 were diagnosed as PTB on initial High resolution computed tomography (HRCT) assessment (Table 1). Out of those 60 patients, only 54 turned out to have pulmonary tuberculosis on final diagnosis (Table 2). The rest of the sixteen were grouped as Non-PTB (non-tubercular pulmonary pathologies/non-pulmonary tuberculosis). Confirmation of the diagnosis was done by one or more of the following: culture for Mycobacterium tuberculosis and PCR tests like cartridge-based nucleic acid amplification test (CB-NAAT) on the sputum done in all cases, and clinical and radiological improvement after anti-tubercular treatment, on follow-up after three months. Culture positivity was seen in 24 patients. Determination of disease activity in others was done using clinical findings, laboratory parameters, response to anti-tubercular treatment, and radiological follow-up over a 4-6 month interval. Those showing clinical improvement and radiographic resolution on follow-up were considered as active cases.

Table 1: Diagnosis of 70 patients with suspected sputum smear-negative PTB based on initial HRCT assessment.

HRCT Diagnosis		No of cases	Percentage %
Pulmonary tuberculosis (PTB)		60	85.71
Non-pulmonary tuberculosis (Non-PTB)	Bacterial pneumonia	3	4.28
	Sarcoidosis	2	2.85
	Septic emboli	2	2.85
	Lung abscess	1	2.85
	ABPA	1	1.42
	Lung cancer	1	1.42
	Total	70	100%

Table 2: Diagnosis of 70 patients with suspected sputum smear-negative PTB based on culture/PCR analysis/Clinical follow up.

Final Diagnosis	No of cases	Percentage%
Pulmonary tuberculosis (PTB) -smear negative	54	77.14
Non-pulmonary tuberculosis (Non-PTB)	Bacterial pneumonia	6	8.57
	Sarcoidosis	3	4.28
	Septic emboli	2	2.85
	Lung cancer	2	2.85
	Lung abscess	1	1.42
	Hypersensitivity pneumonitis	1	1.42
	ABPA	1	1.42
Total	70	100%	

Comparing clinical and laboratory findings in sputum smear-negative, PTB, and non-PTB patients with suspected PTB, a statistically significant correlation was found between pulmonary tuberculosis and symptoms like cough (p=0.0017) and chest pain (p=0.048). A positive Mantoux test result alone was associated with a significant increase in PTB risk (Table 3).

Table 3: Comparison of clinical and laboratory findings in sputum smear-negative PTB and non- PTB in patients with suspected PTB.

Parameters		PTB (n = 54)	Non-PTB (n = 16)	p-value
Clinical	Age	38.35 + 15.514	37.19 + 17.233	0.883
	Female gender	26/54 (48.1%)	5/16 (31.2%)	0.232
	Cough	46 (85.18%)	7 (43.75%)	0.0017
	Sputum	32 (59.25%)	6 (37.25%)	0.1276
	Hemoptysis	5 (9.25%)	1 (6.25%)	1
	Fever (> 37˚C)	19 (35.18%)	9 (56.25%)	0.1337
	Chest pain	21 (38.88%)	2 (12.5%)	0.048
	Loss of weight	6 (11.11%)	1 (6.25%)	1
	Loss of appetite	6 (14.81%)	1 (6.25%)	1
Laboratory	TLC (cells/mm3)	7360.55 +2358.40	10768 + 2469.20	0.001
	ESR (mm/1st hr)	38.80 + 18.312	24.81 + 8.79	0.003
	Mantoux test	16.04 + 5.693	8.56 + 2.421	0

On Comparison of CXR and CT in smear-negative PTB patients: Chest radiograph was within normal limits in 3 patients. However, their subsequent HRCT chest scan had one or more of the following findings: centrilobular nodules, large nodules, tree-in-bud pattern, miliary nodules, and bronchiectasis (Table 4). HRCT detected all centrilobular nodules (75.96%) and bronchial wall thickening (11.11%), completely missing on the CXR chest. The large nodules were seen in 33/55 (61.11%) patients on the HRCT chest, whereas only 24/54 (44.44%) patients showed nodules on CXR. It was more sensitive than the CXR chest is showing all other findings also.

Table 4: Comparison of CXR and CT in smear negative PTB patients (n=54).

FINDINGS	CXR	Percentage	CT	Percentage
Normal	3	5.55	0	0
Centrilobular nodules	0	0	41	75.92
Miliary nodules	1	1.85	2	3.7
Large nodules	24	44.44	33	61.11
Calcified nodules & lesions	3	5.55	12	22.22
Consolidation	27	50	32	59.25
Cavity/abscess	10	18.51	14	25.92
Fibrotic lesions ± bronchiectasis	16	29.62	19	35.18
Bronchiectasis	1	1.85	6	11.11
Bronchial wall thickening	0	0	6	11.11

Pleural effusion	5	9.25	6	11.11
Pleural thickening	1	1.85	7	12.96
Lymphadenopathy	5	9.25	18	33.33

On Comparison of CT findings in smear-negative PTB and non-PTB patients, it was found that the centrilobular nodules, lobar consolidation, large nodules, and tree-in-bud appearance with their location in S1, S2, S1+S2 & S6 on HRCT chest were associated with a significant increase in the risk of PTB ($p<0.05$). The lobular consolidation, mass, and ground-glass opacity on the HRCT chest were associated with a significant increase in the risk of non-PTB patients ($p<0.05$) (Table 5).

Table 5: Comparison of CT findings in smear negative PTB and non-PTB patients (n=70)

CT FINDINGS			PTB (n=54)	Non-PTB (n=16)	p-value
Pulmonary	Nodules	Centrilobular nodules	41 (75.92%)	6 (37.5%)	0.004
		Clustered nodules	0 (0)	1 (6.25%)	0.229
		Miliary nodules	2 (3.70%)	0 (0)	1
		Calcified nodules	10 (18.51%)	1 (6.25%)	0.272
		Large nodules	33 (61.11%)	5 (31.25%)	0.035
		Mass (> 20 mm)	0 (0)	3 (18.75%)	0.01
		Tree-in-bud pattern	31 (57.40%)	1 (6.25%)	0.004
	Lobular consolidation		33 (61.1%)	4 (25%)	0.024
	Lobar consolidation		0 (0)	3 (18.75%)	0.0012
	Interstitial septal thickening		0 (0)	2 (12.5%)	0.05
	Ground glass opacity		1 (1.85%)	4 (25%)	0.008
	Calcified lesions		7 (12.96%)	0 (0)	0.339
	Fibrotic lesions		19 (35.18%)	2 (12.5%)	0.121
	Cavity	Thin walled	11 (78.57%)	0 (0)	0.744
		Thick walled		3 (21.42%)	2 (100%
		Central		4 (28.57%)	1 (50%)
		Peripheral		10 (71.42%)	1 (50%)
		Air fluid level		2 (14.28%)	1 (50%)
		Surrounding consolidation		4 (28.57%)	2 (100%)
	Bronchial Changes	Bronchiectasis	6 (11.11%)	1 (6.25%)	1
		Bronchial wall thickening	6 (11.11%)	0 (0)	0.325
	Main lesion in S1, S2, S1+S2 & S6		41 (75.92%)	4 (25%)	0.0002
Extra-pulmony	Pleura	Pleural effusion	4 (7.40%)	2 (12.5%)	0.614
		Pleural thickening	7 (12.96%)	0 (0)	0.184
	Lymph Nodes	Mediastinal lymphadenopathy	18 (33.33%)	5 (31.25%)	0.671

(S1 = apical segment of right upper lobe; S2 = posterior segment of right upper lobe; S1 + S2 = apico-posterior segment of left upper lobe; S6 = superior segment of right or left lower lobe)

The HRCT chest findings in active and inactive PTB were different. Centrilobular nodules, large nodules, tree-in-bud pattern, and lobular consolidation were more commonly noted in active PTB patients (Figure 1-4). The fibrotic lesions and calcified mediastinal lymph nodes denote inactive PTB. The sensitivity and specificity of the HRCT in determining the disease activity of PTB were 95.65% and 87.5%. The positive predictive and negative predictive values of the HRCT in determining the disease activity of PTB were 97.77%, and 77.77%, respectively. The diagnostic accuracy of HRCT in determining the disease activity of PTB was 94.44% (Table 6)

Table 6: CT findings in active and inactive PTB (n=54)

CT FINDINGS			Active PTB patients (n = 46)	Inactive PTB patients(n=8)
Pulmonary	Nodules	Centrilobular nodules	40 (86.95%)	1* (12.5%)
		Miliary nodules	2 (4.34%)	0 (0)
		Calcified nodules	6 (13.04%)	4 (50%)
		Large nodules	33 (71.73%)	0 (0)
		Tree-in-bud pattern	31 (67.39%)	0 (0)
	Lobular consolidation		33 (71.73%)	0 (0)
	Interstitial septal thickening		0 (0)	0 (0)
	Ground glass opacity		1 (2.17%)	0 (0)
	Calcified lesions		3 (6.52%)	4 (50%)
	Fibrotic lesions		11** (23.91%)	8 (100%)
	Cavity		13 (28.26%)	1 (12.5%)
	Bronchial changes	Bronchiectasis	6 (13.04%)	0 (0)
		Bronchial wall thickening	6 (13.04%)	0 (0)
	Emphysematous change	0 (0)	2 (25%)	
Extra-pulmonary	Pleura	Pleural effusion	4 (8.69%)	0 (0)
		Pleural thickening	2 (4.34%)	5 (62.5%)
	Lymph Nodes	"Mediastinal lymphadenopathy"	18 (39.13%)	0 (0)
		Calcified mediastinal lymph nodes	1 (2.17%)	8 (100%)

* - one case was false positive ** - two cases were false negative

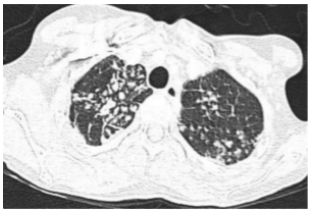

Figure 1 – Axial HRCT section of lung shows multiple discrete and confluent centrilobular nodules (< 8 mm) showing tree-in bud pattern (arrow) scattered in bilateral lungs

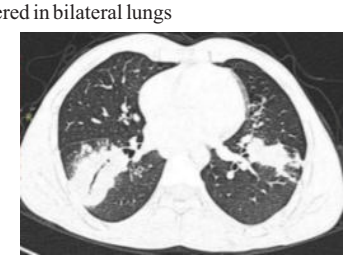

Figure 2 – Axial HRCT section of lung shows lobular consolidation (arrows) involving superior segments of bilateral lower lobes

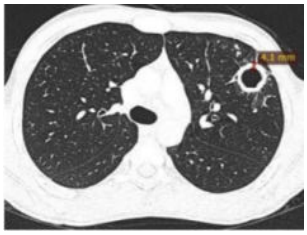

Figure 3 – Axial HRCT section of lung shows the peripheral location of a thin-walled cavity (arrow) in the left upper lobe in a case of smear negative Pulmonary TB.

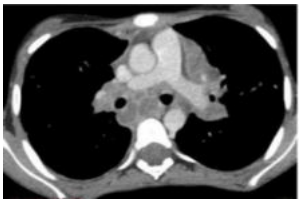

Figure 4 – Axial mediastinal window shows multiple enlarged conglomerates peripherally enhancing lymph nodes(arrow) with central necrosis in pre-vascular, AP window, subcarinal and left hilar location in a case of smear negative PTB.

A combination of five HRCT findings, i.e., centrilobular nodules, large nodules, tree-in-bud pattern, lobular consolidation, and location of the main lesion in S1, S2, S1+S2 had a significant association with smear-negative PTB (<0.05). Based on these HRCT chest findings, diagnostic criteria for diagnosing sputum smear-negative PTB among patients with suspected PTB was proposed by assigning ranks to a combination of findings mentioned above. Patients were assigned a rank from 0 to 3 details of which is explained in Table 7.

Table 7: HRCT diagnostic criteria for diagnosing sputum smear negative PTB.

Rank no.	Inference	HRCT findings required for diagnosis
3	High suspicion of PTB	Presence of at least 3 of the following findings: centrilobular nodules; tree-in-bud pattern; large nodules; lobular consolidation; main lesion in S1, S2, S1+S2 & S6
2	Probable PTB	Presence of at least 3 of the following findings:Presence of at least 3 of the following findings: centrilobular nodules; tree-in-bud pattern; large nodules; lobular consolidation; main lesion in S1, S2, S1+S2 & S6
1	Non-specific or difficult to differentiate from other diseases	No characteristic findings indicating other diseases or findings that are difficult to differentiate from other diseases
0	Other suspected diseases	Some findings indicating other specific diseases

The distribution of suspected smear-negative PTB cases according to ranking using our designed HRCT criteria is shown in Table 8. The sensitivity, specificity, positive and negative likelihood ratios of our HRCT diagnosis is described in Table 9. When rank 3 alone was considered positive, the sensitivity, the specificity, the positive and negative likelihood ratios were 62.96 %, 93.75 %, 10.5, and 0.39, respectively. When rank 2 was considered positive, the sensitivity, the specificity, the positive and negative likelihood ratios were 70.03%, 81.25%, 3.68, and 0.37, respectively. When ≥ rank 1 was considered positive, these values were 100%, 37.5%, 1.58, and 0, respectively.

Table 8: Distribution of suspected smear negative PTB cases according to ranking using our designed HRCT criteria (n=70).

RANK	TOTAL	CASES	NUMBER
		PTB	0
Rank 0	6	Non-PTB	6
Rank 1	23	PTB	16
		Non-PTB	7
Rank 2	6	PTB	4
		Non-PTB	2
Rank 3	35	PTB	34
		Non-PTB	1

Table 9: Sensitivity, specificity, positive likelihood ratio and negative likelihood ratio for each rank of HRCT diagnosis.

Parameters	≥ Rank 1	≥ Rank 2	Rank 3
Sensitivity	100	70.37	62.96
Specificity	37.5	81.25	93.75
Positive likelihood ratio	1.58	3.68	10.5
Negative likelihood ratio	0	0.37	0.39

DISCUSSION:

Globally, tuberculosis incidence is falling at about 2% per year between 2015 to 2019. The health target of United Nations Sustainable Developments Goals (SDGs) is to end Tuberculosis (TB) epidemic by 2030. So, the early diagnosis of Pulmonary tuberculosis (PTB) is critical for effective TB control. The clinical and laboratory findings of PTB are similar to a lot of diseases. The sensitivity of sputum smear examination is very low, especially in mild disease, where it is false negative due to low bacilli load in a sputum sample. The sputum culture takes a long time. So, the patients with suspected PTB and negative sputum smear are a big diagnostic dilemma for clinicians. The criteria for a smear-positive patient cannot be universally used because smear-negative patients have a lower mycobacterial burden.

Presently in our study, the most important criteria for establishing a presumptive diagnosis in smear-negative PTB are based on clinical findings, radiographic signs, risk factors, or a combination of these.

In our study, all patients with suspected PTB and sputum smear-negative were divided into two groups based on final diagnosis as PTB and Non-PTB. Out of 70 patients, fifty-four were proven PTB, out of which only twenty-four showed culture positivity and forty-one showed cartridge-based nucleic acid amplification test (CB NAAT) positivity. The age of the patients ranged from 18-70 years with a mean age of 38.09+_15.8 years, which was similar to that mentioned in the Kanaya et al. study.

Most patients presented with more than one symptom; cough was most frequently reported, followed by sputum production. Chest pain was seen in 21/54 (38.88%) patients. Fever (> 37ºC) was more commonly associated seen in non-PTB patients [1]. We found a statistically significant correlation between smear-negative PTB and symptoms like cough (p=0.0017) and chest pain (p=0.048). This was in agreement with the study done by Samb et al. [2].

The Mantoux test values ranged from 5 mm to 26 mm and were significantly associated with smear-negative PTB (p=0.000). This was in accordance with existing literature [1,3,4]

Patchy consolidation and nodular opacities were commonly noted on chest x-ray (CXR) in 50% and 44.44% of the patients. The cavity was seen only in 18.51% of smear-negative PTB patients. Similar results were obtained by Ebrahimzadeh et al. in their study, who observed cavity in 22% of smear-negative PTB patients compared to 53% of smear-positive PTB patients on chest x-ray [5].

The main role of high-resolution computed tomography (HRCT) is in selecting probable or highly suspicious cases of pulmonary TB with negative sputum smears based on their imaging findings.

In our study, centrilobular nodules were seen in 41/54 (75.92%) of smear-negative patients, and their presence showed a significant association with smear-negative PTB compared to non-PTB patients (p=0.004). Our findings are in accordance with the study by Nakanishi et al. and Tozkoporan et al. [3, 6]. Hatipoğlu et al. found that centrilobular lesions with tree-in-bud appearance and macro nodules are most commonly seen in active cases of PTB [7].

In our study, the presence of large nodules was seen in 33/54 (61.11%)

patients with smear-negative PTB and showed significant association with it (p=0.035).

The tree in bud appearance was found in 31/54 (57.46%) in sputum smear-negative PTB patients. The presence of tree-in-bud appearance had a significant association with smear-negative PTB in our study (p=0.002). The tree-in-bud pattern on computed tomography (CT) was first used by Im et al. for defining the endobronchial spread of pulmonary tuberculosis. Although a reliable criterion for assessing active disease, the tree-in-bud pattern is not pathognomonic for active PTB [8,9].

We observed that lobular consolidation was more commonly seen in smear-negative patients than non-PTB patients (61% Vs. 25%). The presence of lobular consolidation showed a significant association with smear-negative PTB in our study (p=0.0365). Bhalla et al., in their study, stated that the presence of lobular consolidation favors TB, while segmental or lobar consolidation is more likely seen with other bacterial infections [10].

We observed a statistically significant association between lobar consolidation, interstitial septal thickening & ground-glass opacity in non-PTB ($p<0.05$) patients. McGuinness et al. also suggested that bacterial pneumonia follows the lobar or segmental consolidation pattern, while Mycobacterium causes lobular consolidation [11].

The majority of the cavities observed in our study had thin walls and were peripheral in location. Our results agree with the study by Ors et al., which suggested that the thickness of the cavity wall and the distance of the cavity from the main bronchi are two important findings found to be related to the degree of sputum smear positivity and hence bacilli load. This relationship might be explained by the probability of higher bacilli load in cavities with thicker walls [12]. Tozkoparan et al. [6], Nakanishi et al. [3], Caliskan et al. [13], and Ko et al. found the occurrence of cavities to be less frequent in smear-negative PTB patients in their studies.

In our study, the location of the main lesion, such as consolidation and centrilobular nodules in S1, S2, or S1+S2 and S6 lung segments, were commonly associated with smear-negative PTB patients ($p<0.05$). We also found that the location of the cavities in S1, S2, and S1+S2 lung segments were associated with smear-negative PTB (p=0.0509; borderline significant). The location of the cavity in s6 showed no significant association with smear-negative PTB patients. Lee et al. found the location of lesions PTB (both active and inactive) predominantly in S1, S2, or S1+S2 and S6 lung segments in their study [14].

The most common pattern of mediastinal lymph nodes observed in PTB is peripheral rim enhancement with central necrosis on contrast-enhanced scans (15,16). Our study showed a similar pattern of enhancement of mediastinal lymph nodes in 55.55% of patients.

On comparison of chest x-ray and HRCT chest in PTB patients in our study, HRCT chest was superior to chest radiography in assessing the bronchogenic spread of pulmonary tuberculosis, 33/54 patients showed large nodules on CT, whereas only 24/54 patients showed large nodules on chest radiography. HRCT is better than plain chest radiograph in identifying the extent of PTB, especially subtle areas of consolidation, cavitation, bronchogenic and miliary spread [8,9,17]; a similar observation was made in our study. It is also superior to chest radiography in detecting and characterizing mediastinal lymph nodes [18,19]. In our study, lymphadenopathy was seen in 18/54 of PTB patients on CT while it was seen only in 5/54 of patients on chest radiography, re-enforcing the superiority of CT for assessing mediastinal lymph nodes.

The HRCT chest findings in active and inactive PTB were different. We had 46 active and eight inactive cases in our study. Out of 46 active cases, two were false negatives being initially diagnosed as inactive. Out of the eight inactive cases, one case with suspected reactivation was diagnosed as active based on few centrilobular nodules in addition to fibroatelectatic lesions on HRCT but was found to be stable over a six-month follow-up. We compared the HRCT findings in active PTB (n=46) and inactive PTB (n=8). Bhalla et al., in their study, have suggested that the chest x-ray and CT findings help categorize the disease as active TB, indeterminate for disease activity, and inactive TB. [10]. In our study, HRCT findings include centrilobular nodules, large nodules, tree-in-bud pattern, lobular consolidation, cavity, mediastinal lymphadenopathy, bronchiectasis, and bronchial wall thickening were noted more commonly in patients with active PTB. All the patients with inactive PTB showed fibrotic lesions and calcified mediastinal lymph nodes on HRCT.

The sensitivity, specificity, positive predictive & negative predictive value of the HRCT in determining the disease activity of PTB were 95.65%, 87.5%, 97.77% 77.77%, respectively, in our study. The diagnostic accuracy of HRCT in determining the disease activity of PTB was 94.44%.our findings agreed with Wang et al.

A combination of 5 HRCT findings is centrilobular nodules, large nodules, tree in bird pattern, lobular consolidation, and location of the main lesion inS1, S2, or S1+S2 and S6 had a significant association with smear-negative PTB ($p<0.05$) in our study. Based on these HRCT findings, diagnostic criteria for diagnosing sputum smear-negative PTB on HRCT were established in our study. The patients were ranked from 1 to 3 according to a combination of five HRCT findings that were significantly associated with increased risk of pulmonary TB [Table 7]. We found that this ranking was useful to predict the risk of pulmonary TB with good reproducibility.

In our study, when rank 3 alone was considered positive, the sensitivity, specificity, positive likelihood, and negative likelihood ratios for risk of pulmonary TB were 62.96%, 93.75%, 10.5, and 0.39, respectively. When $\geq$ rank 1 was considered positive, the sensitivity, specificity, positive likelihood, and negative likelihood ratios for risk of pulmonary TB were 100%, 37.5%, 1.58, and 0, respectively. Our findings were concordant with the findings of Shaarawy et al. [3] and Nakanishi et al. [4].

CONCLUSION:

The high resolution computed tomography (HRCT) chest is an excellent imaging modality for diagnosing sputum smear-negative active Pulmonary tuberculosis (PTB). The presence of centrilobular nodules, large nodules, tree in bird appearance, lobular consolidation, and location of the main lesion in S1, S2, or S1+S2 and S6 was significantly associated with an increase in the risk factor for smear-negative PTB among suspected PTB. HRCT attains a pivotal role in selecting and segregating probable/ highly suspicious pulmonary TB cases suspected of having active pulmonary TB with negative sputum smears. HRCT can exclude other diseases and accurately predict the risk of PTB even in the setting of sputum smear negativity. In addition, it can select the patients requiring further diagnostic tests and start the anti-tubercular treatment.

REFERENCES:

1. Kanaya AM, Glidden DV, Chambers HF. Identifying pulmonary tuberculosis in patients with negative sputum smear results. Chest. 2001 Aug;120(2):349-55.
2. Samb B, Henzel D, Daley CL, Mugusi F, Niyongabo T, Mlika-Cabanne N, et al. Methods for diagnosing tuberculosis among in-patients in eastern Africa whose sputum smears are negative. Int J Tuberc Lung Dis. 1997 Feb;1(1):25-30.
3. Nakanishi M, Demura Y, Ameshima S, Kosaka N, Chiba Y, Nishikawa S, et al. Utility of high-resolution computed tomography for predicting risk of sputum smear-negative pulmonary tuberculosis. Eur J Radiol. 2010 Mar;73(3):545-50.
4. Shaarrawy H, Zeidan M, Nasr A, Nouh M. Assessment of the role of high-resolution computed tomography in the diagnosis of suspected sputum smear negative active pulmonary TB. Egyptian Journal of Chest Diseases and Tuberculosis. 2013 Apr;62(2):263-8.
5. Ebrahimzadeh A, Mohammadifard M, Naseh G. Comparison of Chest X-Ray Findings of Smear Positive and Smear Negative Patients with Pulmonary Tuberculosis. Iran J Radiol. 2014 Sep;11(4):e13575.
6. Tozkoparan E, Deniz O, Ciftci F, Bozkanat E, Bicak M, Mutlu H, et al. The roles of HRCT and clinical parameters in assessing activity of suspected smear negative pulmonary tuberculosis. Arch Med Res. 2005 Mar-Apr;36(2):166-70.
7. Hatipoğlu ON, Osma E, Manisali M, Ucan ES, Balci P, Akkoclu A, et al. High resolution computed tomographic findings in pulmonary tuberculosis. Thorax. 1996 Apr;51(4):397-402.
8. Im JG, Itoh H, Shim YS, Lee JH, Ahn J, Han MC, et al. Pulmonary tuberculosis: CT findings--early active disease and sequential change with antituberculous therapy. Radiology. 1993 Mar;186(3):653-60.
9. Raniga S, Parikh N, Arora A, Vaghani M, Vora PA, Vaidya V. Is HRCT reliable in determining disease activity in pulmonary tuberculosis?. Indian J Radiol Imaging. 2006 Apr;16(2):221.
10. Bhalla AS, Goyal A, Guleria R, Gupta AK. Chest tuberculosis: Radiological review and imaging recommendations. Indian J Radiol Imaging 2015 Aug;25(3):213-25.
11. McGuinness G, Gruden JF, Bhalla M, Harkin TJ, Jagirdar JS, Naidich DP. AIDS-related airway disease. AJR Am J Roentgenol. 1997 Jan;168(1):67-77. Ors F, Deniz O, Bozlar U, Gumus S, Tasar M, Tozkoparan E, et al.
12. High-resolution CT findings in patients with pulmonary tuberculosis: correlation with the degree of smear positivity. J Thorac Imaging. 2007 May;22(2):154-9.
13. Caliskan T, Ozkisa T, Aribal S, Kaya H, Incedayi M, Ulcay A, et al. High resolution computed tomography findings in smear-negative pulmonary tuberculosis patients according to their culture status. J Thorac Dis. 2014 Jun; 6(6): 706–712.
14. Lee KS, Hwang JW, Chung MP, Kim H, Kwon OJ. Utility of CT in the evaluation of pulmonary tuberculosis in patients without AIDS. Chest. 1996 Oct;110(4):977-84.
15. Jaiswal A, Khanna SP, Menon MP. Computed tomography features of tuberculous

mediastinal lymphadenopathy. Ind Jour Tub. 1992;36:229.
16. Pombo F, Rodríguez E, Mato J, Pérez-Fontán J, Rivera E, Valvuena L. Patterns of contrast enhancement of tuberculous lymph nodes demonstrated by computed tomography. Clin Radiol. 1992 Jul;46(1):13-7.
17. Miller WT. Tuberculosis in the 1990's. Radiol Clin North Am. 1994 Jul;32(4):649-61.
18. Skoura E, Zumla A, Bomanji J. Imaging in tuberculosis. Int J Infect Dis. 2015 Mar;32:87-93.
19. Pastores SM, Naidich DP, Aranda CP, McGuinnes G, Rom WN. Intrathoracic adenopathy associated with pulmonary tuberculosis in patients with human immunodeficiency virus infection. Chest. 1993 May;103(5):1433-7.