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ORIGINAL RESEARCH

Role of High-Resolution Computed Tomography in Predicting Disease Activity in Patients of Pulmonary Tuberculosis

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Abstract

Background: In this study, we wanted to study the radiological findings of pulmonary tuberculosis on high resolution computed tomography (HRCT) scan, and compare the association between high resolution computed tomography findings in pulmonary tuberculosis with sputum positivity.

Materials and methods: This was a hospital based cross-sectional study conducted among 40 patients who presented with pulmonary tuberculosis to the Department of Radiodiagnosis, Government Medical College and Rajindra Hospital, Patiala, after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

Results: The difference of presence of centrilobular nodules in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). The difference of presence of tree in bud pattern in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). The difference of presence of consolidation in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). The difference of presence of ground glass opacity in active and inactive cases of pulmonary TB was statistically insignificant. The difference of presence of lymphadenopathy in active and inactive cases of pulmonary TB was statistically insignificant. Fibrosis and tractional bronchiectasis are best indicators of inactive disease. Certain features such as ground glass opacity, mediastinal lymphadenopathy, emphysema, pleural effusion, calcified granuloma and pleural thickening are seen in both active and inactive cases. In view of delay in sputum culture reports, HRCT has vital role in early diagnosis of TB and hence prevents community spread of disease.

Conclusion: Centrilobular nodules, tree-in-bud pattern, consolidation and cavitation on HRCT are the best indicators of active disease with statistically significant difference between active and inactive cases. Fibrosis and tractional bronchiectasis are best indicators of inactive disease. Certain features such as ground glass opacity, mediastinal lymphadenopathy, emphysema, pleural effusion, calcified granuloma and pleural thickening are seen in both active and inactive cases. In view of delay in sputum culture reports, HRCT has vital role in early diagnosis of TB and hence prevents community spread of disease.

Keywords: High Resolution Computed Tomography, Centrilobular Nodules, Pulmonary Tuberculosis.

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Introduction

Pulmonary TB is caused by mycobacterial species in the *Mycobacterium tuberculosis* complex. *Mycobacterium tuberculosis* is the species responsible for the vast majority of cases, but other species can cause similar disease, including *Mycobacterium africanum, mycobacterium bovis, Mycobacterium microti* and *Mycobacterium canettii*. Air borne mycobacteria are transmitted by droplets of size 1 – 5 μm in diameter, which can remain suspended for several hours in the air when a person with active TB coughs, sneezes, or speaks. Not all individuals exposed to TB get infected. The probability of transmission to exposed individual depends on the environment and duration of exposure, infectiousness of the TB source and the immune status of the exposed individual.[1]

The individuals get infected by inhalation of airborne droplets, which infect alveolar macrophages. The individuals in whom immune system is inadequate at controlling the initial infection leads to development of active TB, this category is referred to as primary TB. The individuals in which immune system is effective at controlling the initial infection, but viable mycobacterium remain dormant and can reactivate at a later time, this category is referred to as post primary TB. The vast majority of infected individuals harbour the infection only at a subclinical level and will never develop symptomatic disease, which is referred to as latent TB infection. The immune response of individual to mycobacteria has important implications for the clinical and imaging appearance of TB, particularly in immunocompromised patients. TB infects an estimated one-third of the world‘s population, thereby making the disease a major public health issue.[1]

Co-infection with HIV and *Mycobacterium tuberculosis* is the strongest known risk factor for both immediate and delayed progression from infection to active TB.[2] The risk of progression to disease for co-infected persons is 5 % – 10 % per year compared with a 5 % – 10 % life-time risk for HIV negative individuals.[3,4] Other known risk factors for development of active TB include conditions that are associated with defects in T-lymphocyte and/or macrophage function, such as malnutrition, drug and alcohol abuse, co-existent medical conditions (e.g., chronic renal failure, diabetes mellitus, silicosis, jejunoileal bypass, and subtotal gastrectomy), and corticosteroid or other immunosuppressive therapy.[5,6]

Active disease may manifest with symptoms that develop during the course of several months which were minimal initially. Typical symptoms of active TB include fever, productive cough, haemoptysis, weight-loss, fatigue, malaise and night sweats.[7]

It is of utmost importance to have a basic understanding of laboratory testing in patients who are suspected of having TB and to integrate the clinical context and relevant laboratory findings and to optimize communication with the referring clinician and provide the best possible patient care. The limitations of laboratory investigations in the form of false negatives and false positives should be considered in offering a differential diagnosis.[8,9]

Specificity varies on the basis of population (i.e., prevalence of non-tuberculous mycobacteria). For the diagnosis of pulmonary TB smear, microscopy and culture of the respiratory specimen (bronchial fluid or sputum) have been recommended while culture has higher diagnostic yield than that of smear microscopy, its turnaround time is approximately 2 - 8 weeks which limits its usefulness as an initial diagnostic test.[10]Although chest radiographs are acceptably good for the diagnosis of active pulmonary TB, minimal exudative TB can be overlooked on standard chest radiography.[11-13]CT is superior to conventional radiographs in detecting activity and CT features of pulmonary TB have been described.[14-16] Narrow collimation and the use of a high spatial frequency reconstruction algorithm are the two most important technical factors that distinguish a thoracic CT examination as an HRCT study.[17] Other technical modifications may be used to enhance the quality of an HRCT examination, such as targeted reconstructions and higher kilovolt (peak)

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or milli amperage values, but these techniques are not required to produce diagnostic-quality HRCT images.[17] In fact, in recent years increasing awareness of the radiation dose attributable to diagnostic imaging, in particular CT, has led a number of investigators to reduce kilo volt (peak) and milli ampere to limit patient radiation dose. In recent years, because of minimal partial volume effect and high resolution power, high resolution computed tomography (HRCT) has superseded conventional chest radiography and standard CT in the evaluation of pulmonary parenchymal disease and localization of disease in the pulmonary lobule. Using these advantages of HRCT, it has contributed in assessment and evaluation of patients of active and inactive pulmonary.[18-24] A basic understanding of pulmonary anatomy is required for accurate HRCT interpretation. Pulmonary anatomy may be broadly divided into the pulmonary gas exchange units and the pulmonary interstitium.

The pulmonary interstitium may be further subdivided into the central peribronchovascular interstitium and the peripheral centrilobular interstitium; these two fiber networks are continuous with one another. The central peribronchovascular interstitium invests the larger central bronchi and vessels near the pulmonary hilum and courses peripherally, producing the peripheral centrilobular interstitium, eventually merging with the sub pleural interstitial fiber network. The latter is located immediately beneath the visceral pleura and extends into the underlying lung parenchyma at various intervals to produce interlobular septa.[10]The secondary pulmonary lobule is defined as the smallest unit of lung function marginated by connective tissue septa; these connective tissue septa are the interlobular septa.[25]

On an average, each secondary pulmonary lobule contains 12 or fewer pulmonary acini. Secondary pulmonary lobules are supplied by an artery and bronchus, termed the centrilobular artery and bronchus. ‘‘The centrilobular artery and bronchus branch dichotomously within the secondary pulmonary lobule, successively producing intralobular arteries and bronchi, acinar arteries, and respiratory bronchioles, eventually terminating in pulmonary gas exchange units.[10] The centrilobular artery and bronchus are approximately 1 mm in diameter and are located about 5 to 10 mm from the visceral pleural surface.[25] Intralobular arteries are slightly smaller, and smaller still are the acinar arteries, which vary in size from 0.3 to 0.5 mm.[25-27]

HRCT Findings in Pulmonary TB

Centrilobular Nodules

Centrilobular nodules are distributed primarily within the center of the secondary pulmonary lobule. Centrilobular nodules range in size from a few millimetres to slightly greater than 1 cm, and may be well-defined or ill-defined, depending on the underlying disease process. A centrilobular nodular distribution may be recognized when nodules are roughly evenly spaced from one another and approach, but do not contact, visceral pleural surfaces; the nodules are usually positioned about 5 to 10 mm from the visceral pleural surface. Because the centrilobular artery and bronchus are the structures that predominate in the center of the pulmonary lobule, diseases affecting these two anatomic structures account for most processes that produce centrilobular nodules on HRCT.[10] Centrilobular nodules may be further characterized by the presence or absence of a branching configuration, so-called _tree-in-bud.(Figure 1)

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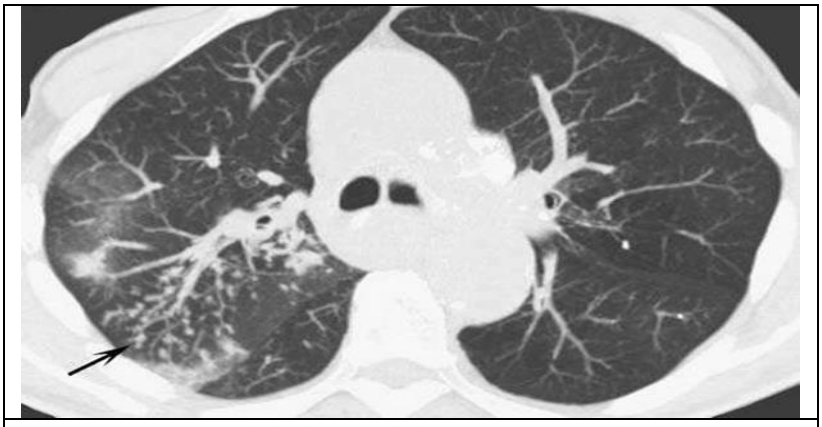

Figure 1 : Centrilobular nodules with tree in bud pattern on HRCT imaging

‘‘Tree-in-bud reflects the presence of impaction of the centrilobular bronchus with mucous, pus, or fluid, resulting in dilation of the bronchus, associated with peribronchiolar inflammation.[28] Dilated, impacted bronchi produce Y- or V-shaped structures on HRCT imaging, and have been likened to a budding tree in spring, hence the term_tree-in-bud.[29-30]

Consolidation

Consolidation is defined as increased attenuation of lung parenchyma which results in obscuration of the underlying vasculature, usually producing air bronchograms.(Figure 2) The presence of consolidation indicates that the air within affected alveoli has been replaced by another substance, such as pus, blood, edema, or cells.[10]

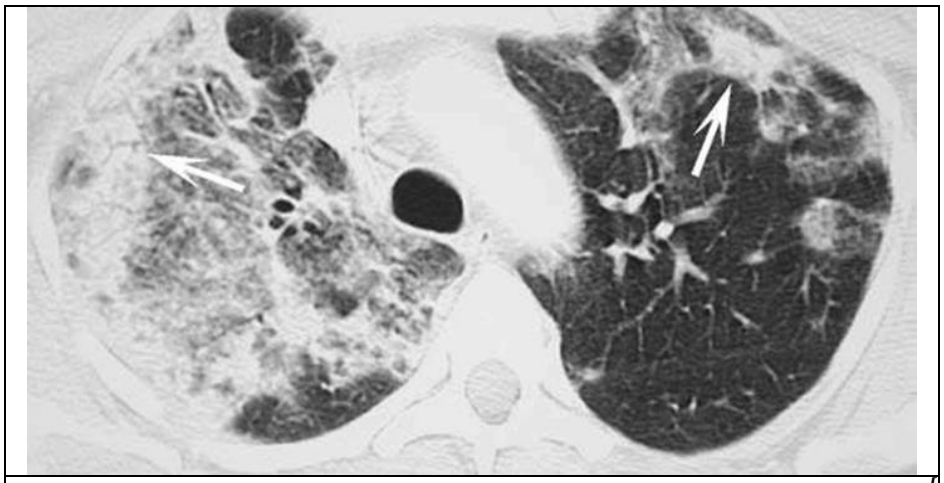

Figure 2 : Consolidation on HRCT imaging (pointed by white arrows)[l]

Aims and Objectives

- To study the radiological findings of pulmonary tuberculosis on high resolution computed tomography scan.
- To find out the association between high resolution computed tomography findings in pulmonary tuberculosis with sputum positivity.

Materials and methods

This was a hospital based cross-sectional study conducted among 40 patients who presented with pulmonary tuberculosis to the Department of Radio Diagnosis, Government Medical College and Rajindra Hospital, Patiala, after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

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Inclusion Criteria

1. Sputum positive cases of pulmonary TB.
2. Clinically suspected cases of pulmonary TB.
3. Patients giving consent to enroll in the study.
4. Age > 18years.

Exclusion Criteria

1. Patients having malignancy.
2. Pregnant females.
3. Patients not giving consent.
4. Age < 18 years.

Statistical Methods

Data was entered in MS Excel and analyzed using Statistical Package for Social Sciences (SPSS) software. Results were presented as tables.

Results

Centrilobular Nodule		**Active**	**Inactive**
Present	No. of patients	20	2
	Percentage	83.33 %	12.5 %
Absent	No. of patients	4	14
	Percentage	16.67 %	87.5 %
Total no of patients		24	16
Percentage		100 %	100 %
P value (Fisher's exact)		0.0001	

Frequency of Distribution of Centrilobular Nodule in Active and Inactive Cases of Pulmonary TB (n = 40)

Tree in Bud		**Active**	**Inactive**
Present	No. of patients	17	3
	Percentage	70.84 %	18.75 %
Absent	No. of patients	7	13
	Percentage	29.16 %	81.25 %
Total no of patients		24	16
Percentage		100 %	100 %
P value (Fisher's exact)		0.003	

Frequency of Distribution of Tree in Bud in Active and Inactive Cases of Pulmonary TB (n = 40)

Consolidation		**Active**	**Inactive**
Present	No. of patients	16	3
	Percentage	66.67 %	18.75 %
Absent	No. of patients	8	13
	Percentage	33.33 %	81.25 %
Total no of patients		24	16
Percentage		100 %	100 %
P value (Fisher's exact)		0.004	

Frequency of Distribution of Consolidation in Active and Inactive Cases of Pulmonary TB (n = 40)

Table 1

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The difference of presence of centrilobular nodules in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). The difference of presence of tree in bud pattern in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). The difference of presence of consolidation in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$).

Cavitation		**Active**	**Inactive**
Present	No. of patients	16	4
	Percentage	66.67 %	25.0 %
Absent	No. of patients	8	12
	Percentage	33.33 %	75.0 %
Total no of patients		24	16
Percentage		100 %	100 %
P value (Fisher's exact)		0.022	

Frequency of Distribution of Cavitation in Active and Inactive Cases of Pulmonary TB (n = 40)

Ground Glass Opacity		**Active**	**Inactive**
Present	No. of patients	7	5
	Percentage	29.16 %	31.25 %
Absent	No. of patients	17	11
	Percentage	70.84 %	68.75 %
Total no of patients		24	16
Percentage		100 %	100 %
P value (Fisher's exact)		0.88	

Frequency of Distribution of Ground Glass Opacity in Active and Inactive Cases of Pulmonary TB (n = 40)

Lymphadenopathy		**Active**	**Inactive**
Present	No. of patients	10	5
	Percentage	41.67 %	31.25 %
Absent	No. of patients	14	11
	Percentage	58.33 %	68.75 %
Total no of patients		24	16
Percentage		100 %	100 %
P value (Fisher's exact)		0.739	

Frequency of Distribution of Lymphadenopathy in Active and Inactive Cases of Pulmonary TB (n = 40)

Table 2

The difference of presence of cavitation in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). The difference of presence of ground glass opacity in active and inactive cases of pulmonary TB was statistically insignificant. The difference of presence of lymphadenopathy in active and inactive cases of pulmonary TB was statistically insignificant.

Fibrosis		**Active**	**Inactive**
Present	No. of patients	8	13
	Percentage	33.33 %	81.25 %
Absent	No. of patients	16	3
	Percentage	66.67 %	18.75 %
Total no of patients		24	16
Percentage		100 %	100 %

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P value (Fisher's exact)		0.008	
Frequency of Distribution of Fibrosis in Active and Inactive Cases of Pulmonary TB (n = 40)			
Tractional Bronchiectasis		**Active**	**Inactive**
Present	No. of patients	7	11
	Percentage	29.16 %	68.75 %
Absent	No. of patients	17	5
	Percentage	70.84 %	31.25 %
Total no of patients		24	16
Percentage		100 %	100 %
P value (Fisher's exact)		0.023	
Frequency of Distribution of Tractional Bronchiectasis in Active and Inactive Cases of Pulmonary TB (n = 40)			
Emphysema		**Active**	**Inactive**
Present	No. of patients	6	9
	Percentage	25.0 %	56.25 %
Absent	No. of patients	18	7
	Percentage	75.0 %	43.75 %
Total no of patients		24	16
Percentage		100 %	100 %
P value (Fisher's exact)		0.093	
Frequency of Distribution of Emphysema in Active and Inactive Cases of Pulmonary TB (n = 40)			
Table 3			

The difference of presence of fibrosis in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). The difference of presence of tractional bronchiectasis in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). The difference of presence of emphysema in active and inactive cases of pulmonary TB was statistically insignificant.

Pleural Effusion		**Active**	**Inactive**
Present	No. of patients	9	3
	Percentage	37.50 %	18.75 %
Absent	No. of patients	15	13
	Percentage	62.50 %	81.25 %
Total no of patients		24	16
Percentage		100 %	100 %
P value (Fisher's exact)		0.29	
Frequency of Distribution of Pleural Effusion in Active and Inactive Cases of Pulmonary TB (n = 40)			
Calcified Granuloma		Active	Inactive
Present	No. of patients	5	8
	Percentage	20.83 %	50.0 %
Absent	No. of patients	19	8
	Percentage	79.17 %	50.0 %
Total no of patients		24	16
Percentage		100 %	100 %
P value (Fisher's exact)		0.11	
Frequency of Distribution of Calcified Granuloma in Active and Inactive Cases of Pulmonary TB (n = 40)			

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Pleural Thickening		Active	Inactive
Present	No. of patients	6	9
	Percentage	25.0 %	56.25 %
Absent	No. of patients	18	7
	Percentage	75.0 %	43.75 %
Total no of patients		24	16
Percentage		100 %	100 %
P value (Fisher's exact)		0.13	

Frequency of Distribution of Pleural Thickening in Active and Inactive Cases of Pulmonary TB (n = 40)

Table 4

The difference of presence of pleural effusion in active and inactive cases of pulmonary TB was statistically insignificant. The difference of presence of calcified granuloma in active and inactive cases of pulmonary TB was statistically insignificant. The difference of presence of pleural thickening in active and inactive cases of pulmonary TB was statistically insignificant.

Discussion

In our study, centrilobular nodules were present in HRCT of 20 cases (83.33 %) out of total of 24 cases of active pulmonary TB and 2 cases (12.5 %) out of total 16 cases of inactive pulmonary TB. The difference of presence of centrilobular nodules in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$).

A positive correlation was found in a study by Hatipoglu et al.[31] (1996) which showed presence of centrilobular nodules were most common finding on HRCT seen in 91 % patients (29 out of 32) and were significantly more common in active pulmonary TB ($p < 0.001$).

In our study, Tree in bud pattern was present in HRCT of 17 cases (70.84 %) out of total of 24 cases of active pulmonary TB and 3 cases (18.75 %) out of total 16 cases of inactive pulmonary TB. The difference of presence of tree in bud pattern in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). A study was done by Raniga et al.[32] (2006) which reported that the tree-in-bud pattern, suggestive of endobronchial spread, and hence active disease, was the most common and characteristic of the findings on HRCT.

In our study, consolidation was present in HRCT of 16 cases (66.67 %) out of total of 24 cases of active pulmonary TB and 3 cases (18.75 %) out of total 16 cases of inactive pulmonary TB. The difference of presence of consolidation in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). A study conducted by Tozkoparan et al.[33](2005) showed that presence of consolidation inactive and inactive TB patients was statistically significant ($p < 0.017$).

In our study, cavitation was present in HRCT of 16 cases (66.67 %) out of total of 24 cases of active pulmonary TB and 4 cases (25 %) out of total 16 cases of inactive pulmonary TB. The difference of presence of cavitation in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). A study conducted by Tozkoparan et al.[33] (2005) showed that presence of cavitation in active and inactive TB patients was statistically significant ($p < 0.001$).

In our study, fibrosis was present in HRCT of 13 cases (81.25 %) out of total of 16 cases of inactive pulmonary TB and 8 cases (33.33 %) out of total 24 cases of active pulmonary TB. The difference of presence of fibrosis in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). A positive correlation was found in a study by Hatipoglu et al.[31] (1996) which showed presence of fibrotic changes and bronchovascular distortion were significantly more common in inactive pulmonary TB ($p < 0.001$).

In our study, tractional bronchiectasis was present in HRCT of 11cases (68.75 %) out of total

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of 16 cases of inactive pulmonary TB and 7 cases (29.16 %) out of total 24 cases of active pulmonary TB. The difference of presence of tractional bronchiectasis in active and inactive cases of pulmonary TB was statistically significant ($p < 0.05$). A similar correlation was seen in the study conducted by Majmudar et al.[34](2017) that showed presence of tractional bronchiectasis in 64 % cases (18 out of 28) of inactive pulmonary TB in comparison to 18.1 % cases (4 out of 22) of active pulmonary TB, suggestive in active disease.

In our study, emphysema was present in HRCT of 9 cases (56.25 %) out of total of 16 cases of inactive pulmonary TB and 6 cases (25 %) out of total 24 cases of active pulmonary TB. The difference of presence of emphysema in active and inactive cases of pulmonary TB was statistically insignificant. A study conducted by Tozkoparan et al.[33](2005) showed that presence of emphysema in active and inactive TB patients were statistically not significant.

In our study, pleural effusion was present in HRCT of 9 cases (37.5 %) out of total of 24 cases of active pulmonary TB and 5 cases (18.75 %) out of total 16 cases of inactive pulmonary TB. The difference of presence of pleural effusion in active and inactive cases of pulmonary TB was statistically insignificant. A similar correlation was found in a study by Nakanishi et al.[35] (2010) which showed that presence of pleural effusion was not significantly associated with active or inactive pulmonary TB.

Conclusion

HRCT can be important in the diagnosis and management as it can differentiate active from inactive disease with greater sensitivity. Centrilobular nodules, tree-in-bud pattern, consolidation and cavitation on HRCT are the best indicators of active disease with statistically significant difference between active and inactive cases. Fibrosis and tractional bronchiectasis are best indicators of inactive disease. Certain features such as ground glass opacity, mediastinal lymphadenopathy, emphysema, pleural effusion, calcified granuloma and pleural thickening are seen both active and inactive cases. In view of delay in sputum culture reports, HRCT has vital role in early diagnosis of TB and hence prevents community spread of disease.

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