INTRODUCTION

Worldwide, 1.7 million people die of tuberculosis each year,1 with nearly 9x10^6 new cases of active tuberculosis (TB) are diagnosed, rising at an alarming rate of one percent per annum.2 Majority i.e. 95% of tuberculosis cases and 98% of deaths due to tuberculosis occur in impoverished countries of Asia, Africa and South America.3 Among these regions, 44% of Southeast Asian population is tuberculosis infected.3 Microbio-logical detection of Acid Fast Bacillus (AFB) remains the gold standard for diagnosis of active tuberculosis; the sensitivity of sputum smear for AFB is 46-74%, and that of the sputum culture is 2-95% with active pulmonary disease.4 The national data documents a yield of 10-22% for smear positivity in active pulmonary tuberculosis in adults.5-6

Chest radiography remains the foremost imaging technique in the evaluation of pulmonary TB. It is unsurpassed in the amount of information it yields in relation to its cost, radiation dose, availability, and ease of performance. However, plain chest radiograph-based diagnosis is correct in only 34% and 59% cases of primary pulmonary TB and postprimary pulmonary TB respectively.7 High Resolution Computed Tomography (HRCT) has been found to be more sensitive than chest radiograph in the detection of minimal exudative lesions,8 subtle or occult parenchymal disease and in assessing disease activity in pulmonary TB.9 In one study, the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of HRCT in detecting disease activity were 88%, 88%, 92%, 83% and 88%, respectively.10 More so, HRCT is more sensitive in detection of miliary nodules;11 to correlate underlying pathomorphological processes,12 mode of spread of the disease and sequential morphological changes after anti-tuberculosis chemotherapy.13 Though the chest radiography can demonstrate cavitation in 40-87% of patients, HRCT chest has proved to be more accurate in detection of cavitation, particularly in cases complicated by extensive fibrosis and architectural distortion.7,14,15 Recently, a relationship has also been reported between morphological findings on HRCT and the number of acid-fast bacilli on sputum smears in patients with pulmonary tuberculosis.16

ABSTRACT

Objective: To determine the High Resolution Computed Tomographic (HRCT) patterns in adults with Acid Fast Bacillus (AFB) positive new cases of Pulmonary Tuberculosis (PTB).

Study Design: A descriptive case series.

Place and Duration of Study: The study was carried out at the Department of Pulmonology and Department of Radiology, Military Hospital, Rawalpindi, from June 2006 to August 2007.

Methodology: Fifty adults with AFB positive new pulmonary tuberculosis were included in the study, while PTB cases in the retreatment category, Multi Drug Resistant (MDR) tuberculosis, PTB with Chronic Obstructive Airways Disease (COPD), pneumoconiosis, Diffuse Parenchymal Lung Diseases (DPLDs) etc. were excluded. All cases underwent HRCT chest with 2 mm collimations at 10 mm intervals. Relevant data was collected on a pre-designed patient proforma.

Results: The mean age was 40.18 ± 14.55 years with 88% males; 46% and 30% samples were sputum and endobronchial washings smear positive for AFB respectively, while the rest were culture positive. HRCT findings included centrilobular nodules in 92% cases, lobular consolidation in 84%, cavitation in 76%, ‘tree-in-bud’ appearance in 68%, lymphadenopathy in 8% and miliary nodules in 4% cases. HRCT patterns included centrilobular nodules and lobular consolidation in 80% cases, while centrilobular nodules with cavitation and centrilobular nodules with ‘tree-in-bud’ appearance were noted in 72% and 68% patients respectively. Thirty two (64%) cases had centrilobular nodules, cavitation and lobular consolidations and about half cases had centrilobular nodules, ‘tree-in-bud’ appearance and lobular consolidation.

Conclusion: Centrilobular nodules and lobular consolidations (80%), centrilobular nodules with cavitation (72%) and centrilobular nodules with ‘tree-in-bud’ appearance (68%) were the most common HRCT patterns in adults newly diagnosed with pulmonary tuberculosis.

Key words: Pulmonary tuberculosis. High resolution CT (HRCT) patterns. AFB positive. Centrilobular nodules.
Although characteristic HRCT findings of pulmonary TB have been described in varied international studies, a similar data in the local patients is non-existent. By identification of these distinctive HRCT patterns, in appropriate clinical settings with atypical or seemingly inactive X-ray chest features and smear negative PTB; the clinician can reach the presumptive diagnosis of active tuberculosis and start empirical therapy.

The purpose of this study was to determine HRCT patterns in adults with AFB positive new pulmonary tuberculosis in adult patients.

**METHODOLOGY**

This case series was conducted at the Department of Pulmonology and Department of Radiology, Military Hospital, Rawalpindi, from June 2006 to August 2007. Fifty adults, 14-75 years of age of either gender reporting to the department of pulmonology (indoor or outdoor) were sequentially enrolled by convenient sampling. Only new (a patient who had never used anti-tuberculosis drugs in the past or has used it for less than four weeks), AFB positive (on sputum or endobronchial washings smear or culture) pulmonary tuberculosis cases were included. AFB positive PTB cases in any retreatment category, Multi-Drug Resistant (MDR) tuberculosis (both primary and secondary) and PTB with Chronic Obstructive Airways Disease (COPD), pneumoconiosis, Diffuse Parenchymal Lung Diseases (DPLDs) were excluded. Pregnant patients (1st and 2nd trimester), patients unable to hold breath (interpretation of fine lesions made difficult by motion artifact) and those with history of allergic reaction to either ionic or non-ionic contrast were also excluded from the study.

All enrolled patients were asked to avoid anything oral intake for at least 2 hours before the procedure. HRCT chest was done with Toshiba GX – Express Single Slice Scanner, using the following protocol: Serial, thin-section slices were taken in supine position at held inspiration, with 2 mm collimation at 10 mm intervals from apices to the hemidiaphragms. All images were reconstructed on a high-resolution bone algorithm without targeting. The scans were photographed with both mediastinal (window width [WW] 250-400 Hounsfield units; window length [WL], -10 to 50 Hounsfield Units (HU)) and lung (WW 1000; WL 700 HU) windows. Intravenous non-ionic contrast was given manually as bolus dose of 50 cc in PTB cases with associated lymphadenopathy to look for areas of low attenuation.

All the HRCT scans were assessed prospectively by one consultant radiologist. The pattern, extent and severity of HRCT findings were recorded. The patterns included micronodules (< 10 mm in diameter), nodules (1-2 cm in diameter), masses (> 3 cm in diameter), lobular consolidation (an area of increase opacity with obscuration of underlying bronchovascular markings, 10-20 mm in size), ground glass attenuation (an area of increased opacity without obscuration of underlying bronchovascular markings) and irregular lines. Micronodules were further sub-classified as (a) centrilobular: well-defined lesions 2-4 mm in size, related to a terminal or respiratory bronchiole in secondary lobule but separated by more than 2 mm from the pleural surface or interlobular septa; while ‘tree-in-bud’ appearance as a branching, linear structure with more than one contiguous branching site, (b) acinar: 6-10 mm in diameter and poorly defined and (c) milliary: 1-2 mm symmetric and bilateral randomly distributed. Lymphadenopathy was considered present if the short axis diameter was larger than 10 mm.

All HRCTs were done within one month of the start of anti-tuberculosis therapy. All the patients also underwent X-ray chest, Mantoux test, blood complete picture, ESR, C-reactive protein and blood sugar. The data was recorded on a preformed patient proforma and informed consent was taken from all patients after complete description of the HRCT procedure. Data was processed on SPSS version 10 and descriptive statistics like gender and frequency of different HRCT patterns, was described in percentages and frequencies; t-test was applied to determine statistically significant difference between X-ray and HRCT for the detection of cavitation and bilateral lung involvement and p-value of <0.05 was considered significant.

**RESULTS**

A total of 50 patients were studied, with a mean age of 40.18 ± 14.55 years. Forty four (88%) cases were males. The mean Hb% was 11.81 ± 1.52 gm with mean ESR fall at the end of 1st hour of 43.82 ± 23.63 mm. Mantoux test was positive in 68% (n=34) cases. Twenty three (46%) cases were sputum smear positive for AFB, while endobronchial washings smear was positive for AFB in 15 (30%) cases. Culture was positive for AFB in an additional 10% and 14% cases of sputum and endobronchial samples respectively.

Unilateral lesions in right and left lung fields were noted in 24% (n=12) and 22% (n=11) cases respectively on X-ray chest as compared to 6% and 8% cases on HRCT respectively. Twenty seven (54%) had involvement of both lung fields on X-ray chest as compared to 86% (n=43) on HRCT. The difference was found to be statistically significant (p < 0.05). Cavitation was detected in 38 (76%) cases on HRCT as compared to 20 (40%) patients on X-ray chest (p < 0.05).

Among the different individual, HRCT findings of active PTB, centrilobular nodules were noted in 92% (n=46) cases, lobular consolidation in 84% (n=42), cavitation in 76% (n=38) and ‘tree-in-bud’ appearance in 68% (n=34). Lymphadenopathy and milliary nodules were
seen in 8% and 4% cases respectively. Four patients with lymphadenopathy showed non-enhancing lymph nodes, while central hypo-attenuation suggestive of PTB was seen in two cases. None had complete normal HRCT chest.

The most commonly found HRCT patterns (a combination of 2 or more individual active radiological lesions) are shown in Table 1.

Few representative HRCT slices are shown in Figures 1, 2 and 3 depicting classical HRCT features of active pulmonary tuberculosis.

**Table 1:** Common HRCT patterns in AFB positive new pulmonary tuberculosis cases.

<table>
<thead>
<tr>
<th>Common HRCT patterns</th>
<th>% Cases</th>
<th>Cases</th>
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<tbody>
<tr>
<td>1. Centrilobular nodules + Cavitation + Lobular consolidation</td>
<td>64%</td>
<td>(32)</td>
</tr>
<tr>
<td>2. Centrilobular nodules + 'tree-in-bud’ appearance + Lobular consolidation</td>
<td>54%</td>
<td>(27)</td>
</tr>
<tr>
<td>3. Centrilobular nodules + Cavitation + 'tree-in-bud’ appearance</td>
<td>48%</td>
<td>(24)</td>
</tr>
<tr>
<td>4. Centrilobular nodules + Lobular consolidation</td>
<td>80%</td>
<td>(40)</td>
</tr>
<tr>
<td>5. Centrilobular nodules + Cavitation</td>
<td>72%</td>
<td>(36)</td>
</tr>
<tr>
<td>6. Centrilobular nodules + 'tree-in-bud’ appearance</td>
<td>68%</td>
<td>(34)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Thoracic tuberculosis can present radiologically as a poorly defined opacity, consolidation, single or multiple cavities, miliary nodules, macro-nodular infiltrates (tuberculomas), mass-like lesions, pleural effusions, mediastinal/hilar lymphadenopathy, and rarely as ARDS and pneumothorax. HRCT is more sensitive than chest radiograph in differentiating between active and inactive tuberculous lesions and is 98% sensitive to detect endobronchial spread as compared to 19-58% on chest radiograph.

HRCT findings of newly diagnosed active pulmonary tuberculosis as reported by Im and colleagues were centrilobular nodules 95%; bronchial wall thickening 73%; poorly defined nodules 61%; cavitation 51% and lobular consolidations in 41% cases.13 Lee et al. described presence of centrilobular nodules in 92%, acinar nodules in 61%, macronodules in 54%, lobular consolidation in 52%, cavitation in 36%, mediastinal lymphadenopathy in 8% and miliary nodules in 3% cases of adults with active pulmonary tuberculosis.18 In a recent study of patients with sputum positive tuberculosis by Raniga and colleagues, 92% had HRCT findings of bronchogenic spread of the disease and 4% had miliary tuberculosis.4 Centrilobular nodule with branching linear structure/’tree-in-bud’ appearance was seen in 80%, cavitation in 64%, consolidation in 52% and poorly defined nodule in 40% cases.

In this study, HRCT findings of newly diagnosed AFB positive PTB cases were mostly comparable to the above-mentioned studies. Centrilobular nodules were the most common finding (92%), which was similar to the reported prevalence of 95%, 92% and 92% by Im et al., Lee et al. and Raniga et al. respectively.4,13,18 Lobular consolidations were noted in 84% in PS, which is more frequent as compared to the studies by Lee et al. (52%), Im et al. (41%) and Raniga et al. (52%).4,13,18 The probable reason was inclusion of large ill-defined nodules as consolidations in the present study and
Nasir et al. described, along with centrilobular nodules in the studies by
Lee et al. and Raniga et al. The incidence of mediastinal lymphadenopathy (8%) and miliary nodules (4%) was similar to the study by Lee and colleagues.

HRCT findings in active tuberculosis include patchy, frequently peribronchial, unilateral or bilateral airspace consolidation, cavitation—thick or thin walled, scattered airspace nodules, centrilobular branching structures / 'tree-in-bud' appearance, miliary disease, pleural effusion, empyema and bronchopleural fistula, and low density hilar/mediastinal lymphadenopathy. Lesions in and around the small airways are the most characteristic CT feature of early active tuberculosis and a heterogeneous, poorly marginated opacity/consolidation, usually in apical or posterior segment of upper lobes and superior/apical segments of lower lobes is the earliest finding of postprimary PTB.

Cavitation in PTB implies a high bacillary burden, high infectivity and associated with endobronchial spread, tuberculous empyema, hematogenous dissemination and pulmonary artery pseudoaneurysm formation. Presence of cavitation with consolidation is also related to smear positivity. Tuberculous cavity develops within a consolidated segment as the caseation necrosis erodes into the bronchial tree, expelling liquefied debris. On HRCT, cavities due to TB can be thick or thin walled and may have smooth or irregular margins. Thick walled cavities probably represent early stages of necrotizing consolidation and may resolve completely, leave a scar, become thin walled or remain open at the end of treatment. However, disease activity cannot be determined on the basis of CT appearance of the cavity alone, and diagnosis must be made from the results of sputum cultures and serial radiographic analysis. Presence of multiple cavities (especially if more than three) in an area of consolidation is found more frequently in PTB than in any other lesion. HRCT is more sensitive than plain radiography in the detection of small cavities, particularly at the apices, lung bases, paramediastinal and retrocardiac locations. Air-fluid levels in tuberculous cavities are regarded unusual and signify superimposed bacterial or fungal infection. In the present cases, the cavitation was both thick and thin walled (Figures 1 and 3), however, inner borders were always smooth and regular.

Endobronchial spread is detected on X-ray chest in 19-58% cases and by HRCT in up to 98%. It results after breakdown of a pulmonary cavitory lesion or from the breakdown of a lobar infection or rupture of an infected lymph node into the bronchus. On chest X-ray, endobronchial spread is associated with poorly defined pulmonary nodules varying between 5 and 10 mm in size. While on HRCT, early features of endobronchial spread are poorly defined centrilobular nodules, or rosettes of nodules, 2-10 mm in diameter, branching centrilobular opacities, also called as 'tree-in-bud' appearance. In comparison to small nodules of miliary tuberculosis, these nodules are non-uniform in size and unevenly distributed. With more advanced disease, the centrilobular opacities coalescence to form focal areas of consolidation.

Cylindrical nodules correspond to inflammatory lesion in the bronchioles and peribroncholar alveoli, while branching linear lesions or 'tree-in-bud' appearance denotes caseation material filling the bronchioles and alveolar ducts. Although 'tree-in-bud' appearance has high sensitivity for the diagnosis of active tuberculosis, its specificity is low. This pattern is now recognized as a CT manifestation of many diverse entities like peripheral airway diseases such as infection (bacterial, fungal, viral, or parasitic), congenital disorders, idiopathic disorders (obliterative bronchiolitis, panbronchiolitis), aspiration or inhalation of foreign substances, immunologic disorders, connective tissue disorders and peripheral pulmonary vascular diseases such as neoplastic pulmonary emboli. Poorly defined nodule or lobular consolidation usually consists of central granuloma with caseation necrosis and a less dense peripheral rim of non-specific inflammation.

As the tuberculosis remits, there is gradual disappearance of lobular consolidation, poorly defined nodules, and centrilobular nodules or branching linear structures in that order. Resolution of lobular consolidation starts at the periphery with eventual transformation into a poorly defined nodule or branching linear lesion. Centrilobular nodules and branching linear structures ('tree-in-bud' appearance) seen on initial CT scan gradually decrease in prevalence and usually disappear after 12 months of treatment. It is worth stressing that well-defined as compared to poorly-defined centrilobular nodules; bronchiectasis and acinar nodules can be found in patients with inactive tuberculosis similar to those with active tuberculosis. However, if these are associated with consolidation or cavity formation, it suggests the diagnosis of active tuberculosis. Other findings of inactive or stable-state pulmonary tuberculosis on HRCT scan include areas of irregular lines and calcified nodules along with distortion of bronchovascular bundles, and paracatricial emphysema.

Presence of an individual HRCT finding, though very sensitive, but is very non-specific and thus presence of constellation/combination of active tuberculosis findings called HRCT patterns in this study were sought. Common HRCT patterns with combination of 2 or more findings of active PTB noted in the present study are shown in Table I. In various studies, the combination of cylindrical nodules and tree-in-bud appearance was
identified as the most characteristic CT feature of active tuberculosis disease. However, in this study, centrilobular nodules along with consolidation (80%) and centrilobular nodules with cavitation (72%) were more frequent than centrilobular nodules and tree-in-bud (68%).

This study had few limitations. First, the total number of patients was comparatively small. Secondly, majority of cases were males, so gender comparison of HRCT patterns was not possible. Thirdly, only one radiologist of sufficient experience was available to study, the HRCT frames, which can be a source of pattern recognition bias.

CONCLUSION

The common HRCT patterns in adults with AFB positive new pulmonary tuberculosis included centrilobular nodules and lobular consolidations (80%), centrilobular nodules with cavitation (72%) and centrilobular nodules with tree-in-bud (68%). Thirty-four (64%) cases had centrilobular nodules, cavitation and lobular consolidations, while more than half cases had centrilobular nodules, tree-in-bud and lobular consolidation.

Most of adult AFB positive new pulmonary tuberculosis cases had two or more radiological features of active disease on HRCT. In appropriate clinical settings with atypical or seemingly inactive X-ray chest features and smear negative PTB; the clinician can reach the presumptive diagnosis of active tuberculosis and start empirical therapy.

REFERENCES