

High-Resolution Computed Tomography Evaluation of Lung Parenchymal Changes in Symptomatic HIV-Seropositive Individuals

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Abstract

Introduction: Pulmonary diseases are the leading cause of morbidity and mortality, and one of the frequent cause of hospital admission in HIV-infected people worldwide. High-resolution computed tomography (HRCT) is a very sensitive tool for accurate assessment and characterization of diffuse lung diseases.

Purpose: The purpose of this study is to characterize pulmonary diseases in HIV-seropositive patients presenting with the chest complaints using HRCT and to correlate the radiological findings with a CD4 count of the patient.

Materials and Methods: The study was conducted on 61 HIV-seropositive patients from February 2016 to September 2017 presented with chest symptoms on 128-slice SIEMENS somatom AS definition machine. Computed tomography-guided biopsy and bronchoalveolar lavage were performed in few cases.

Results: Maximum number of patients was in the age group 20–40 years (64%). Out of 61 patients, 43 (70%) were male, and 18 (30%) were female. In our series of 61 patients, 33 (54%) patients were diagnosed as having pulmonary tuberculosis (TB) followed by fungal infection in 9.8% of the patients and interstitial lung disease in 6.5% patients. Bacterial pneumonia, bronchiolitis obliterans, Kaposi sarcoma, and pulmonary thromboembolism were found in 1.6% of patients each. Sensitivity and specificity to detect pulmonary TB by HRCT were found to be 96.5% and 84.3%, respectively.

Conclusion: HRCT is a very sensitive tool for detection and characterization of lung parenchymal changes that help clinicians develop a focussed approach in patient management.

Key words: High-resolution computed tomography, Human immunodeficiency virus, Interstitial lung disease, Pulmonary tuberculosis, Pneumocystis jiroveci pneumonia

INTRODUCTION

About 36.7 million people worldwide are suffering from HIV infection and associated complications.^[1] An estimated 2.12 million people in India are living with HIV infection.^[2]

HIV infection causes an alteration in several lines of host defenses in the lung and respiratory tract that contribute to an increased risk for lung complications. An incidence of 20–25 episodes per 100 hospital admissions per year has been observed.^[3] Many well-described infectious diseases, cancers, and other pulmonary diseases occur with increased frequency in this population. The majority of the pulmonary complications of HIV-positive patients are infectious in origin which depends mainly on the CD4 count, different disease spectrum is seen at a different range of CD4 count of the patient.^[4,5] With the introduction of highly active antiretroviral therapy, survival of HIV-positive patients has also increased and thus the

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range of pulmonary manifestations. All of these factors underscore the importance of understanding pulmonary diseases in HIV-infected patients and of developing a practical approach for chest imaging studies.

The risk of developing tuberculosis (TB) is estimated to be between 16 and 27 times greater in people living with HIV than among those without HIV infection. In 2015, there were an estimated 10.4 million cases of TB disease globally, including 1.2 million (11%) among people living with HIV. Almost 60% (57%) of TB cases among people living with HIV were not diagnosed or treated, resulting in 390,000 TB-related deaths among people living with HIV in 2015.^[6]

Conventional radiography has low sensitivity and specificity and at many times does not lead to a conclusive diagnosis. HRCT of lung provides detailed visualization of lung parenchyma and can characterize diseases according to pattern and distribution which can help in formulating a differential diagnosis.^[7,8] Hence, my study is intended to document these radiological findings and correlate them with patient's CD4 counts.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Radio-Diagnosis, Pt. Jawahar Lal Nehru Memorial Medical College and Dr. B.R.A.M. Hospital, Raipur (Chhattisgarh), between February 2016 and September 2017 on 61 HIV-seropositive patients who presented with chest complaints.

A thorough clinical history of all the HIV-positive patients presenting with pulmonary disease was taken. Duration of symptoms was also recorded. Then, a meticulous record of all the available laboratory investigations including HIV status, CD4 counts, routine blood examination, sputum examinations, pleural fluid analysis, and other available investigations was kept. Chest X-rays (CXR) of the patients were studied for the presence of any abnormality.

HRCT scans of the chest were performed on 128-slice SIEMENS somatom definition AS machine.

HRCT Imaging Protocol

The procedure and objectives of performing the high-resolution computed tomography (CT) scan were explained to the patient, and written consent of patient was taken. The patient was explained and demonstrated the procedure of breath holding during the acquisition of HRCT scans.

The patient was kept supine on the gantry table and was scanned cephalocaudal in the axial axis. Scans obtained

with patients supine were adequate in most instances. The scanogram or tomogram was first taken, and then the whole lung was scanned from apex to the base. The scans were performed on 128-slice SIEMENS CT scanner using the following protocol.

Collimation = 1 mm

Feed = 10 mm

KVp = 120–140

mA = 250

Pitch = 6

High-spatial-frequency algorithm was used. It reduces image smoothening and increases spatial resolution and making structures appear sharper. Thus, small vessels and bronchi are better seen in HRCT.

Statistical Methods

Data were expressed as a percentage and mean \pm standard deviation Kolmogorov–Smirnov analysis was performed for checking the linearity of the data. Student's *t*-test correlation analysis was used to check the difference between two parameters in parametric data. Fischer's exact test or Chi-square test was used to analyze the significance of the difference between frequency distribution of the data. ROC curve was plotted for prognostic significance. Correlation analysis was performed using Pearson's correlation. $P < 0.05$ was considered as statistically significant. Microsoft® Inc. USA was used to perform the statistical analysis.

RESULTS

The number of patients included in this study was 61. A maximum number of patients was in the age group 20–30 and 31–40 year. About 64% of patients were 20–40 year old, and only 6% were more than 60-year-old. Out of 61 patients, 70.5% were male, and 29.5% were females. The ratio of male-to-female was 2.3:1.

Maximum 54% HIV patients presented with TB followed by 9.8% fungal infection (including pneumocystis jiroveci pneumonia [PJP], cryptococcosis). Usual interstitial pneumonia (UIP) pneumonia was noted in 6.5% cases (including bronchiolitis obliterans organizing pneumonia [BOOP] and UIP). Bacterial pneumonia, bronchiolitis obliterans, Kaposi sarcoma, and pulmonary thromboembolism were noted in 1.6% cases each. However, 18% of study participants did not reveal any significant abnormality.

Maximum 47.5% patients were having CD4 count in the range of 200–499 cells/mm³ and nearly 34.4% patients have CD4 count <200 cell/mm³.

Out of 100, 63.9% maximum number of patients was identified to have airspace nodules followed by lymphadenopathy in 57.4% cases while 42.6% of patients were identified to have consolidation.

Variable size cavitations were found in 13.1% of patients. Ground-glass opacity and lung cyst were evident in 19.7% and 6.5% of patients, respectively.

Pleural effusion was found in 26.3% of patients, and bronchiectasis was noted in 31.1% of patients.

In our study, among pulmonary TB patients, maximum 84% patients demonstrated airspace nodules followed by lymphadenopathy (75.7%), consolidation (51.5%), pleural effusion (33.3%), bronchiectasis (24.2%), cavitation (21.2%), and ground-glass opacity (18.2%). Cavitation and bronchiectasis were found to be more frequent in TB patients.

Lobar consolidation was seen more in bacterial pneumonia patients. However, diffuse ground-glass opacity and lung cyst were found to be a more consistent feature in PJP patients.

The sensitivity and specificity to detect pulmonary TB by HRCT were found to be 96.5% and 84.3%, respectively.

We compared the CD4 counts with different outcomes (i.e., death, deterioration, and improvement on follow-up). The mean CD4 count was found to be lower in patients with death, poor treatment responders, and the highest with clinical symptomatic improvement; however, the difference failed to reach statistical significance ($P < 0.0001$).

Prognostic significance of CD4 count was demonstrated using ROC curves in which 66.9% area comes under the curve with a sensitivity and specificity 72.5% and 62.5%, respectively.

DISCUSSION

The descriptive study of “HRCT evaluation of lung parenchymal changes in symptomatic HIV-seropositive individuals” was conducted in the Department of Radio-diagnosis, Pt. Jawahar Lal Nehru Memorial Medical College and associated Dr B.R. Ambedkar Memorial Hospital, Raipur (Chhattisgarh), from February 2016-September 2017 on 61 HIV-seropositive patients who presented with the chief complaints of chest symptoms of various age groups. Most of the diagnosis was made on the radiological basis along with clinical and laboratory investigations available. Bronchoscopic lavage and CT-guided lung biopsy were performed in a small number of cases.

A maximum number of patients was in the age group 20–40 years (64%) [Figure 1]. Out of 61 patients

included in our study, 43 (70%) were male, and 18 (30%) were female. Male-to-female ratio was 2.3:1 [Figure 2].

Out of 61 cases in the study, 47.5% patient's CD4 count was in the range of 200–499, and about 34.4% patient's CD4 count was below 200 cells/mm³ [Figure 3].

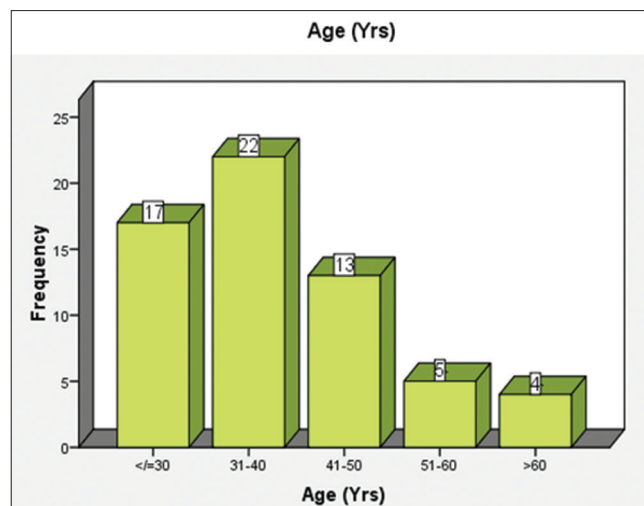


Figure 1: Distribution of HIV-positive patients according to age

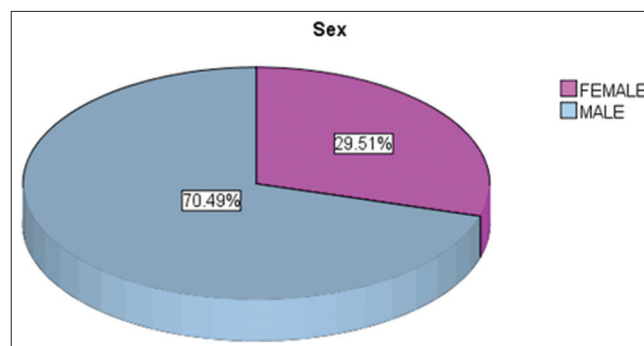


Figure 2: Distribution of HIV-positive patients according to gender

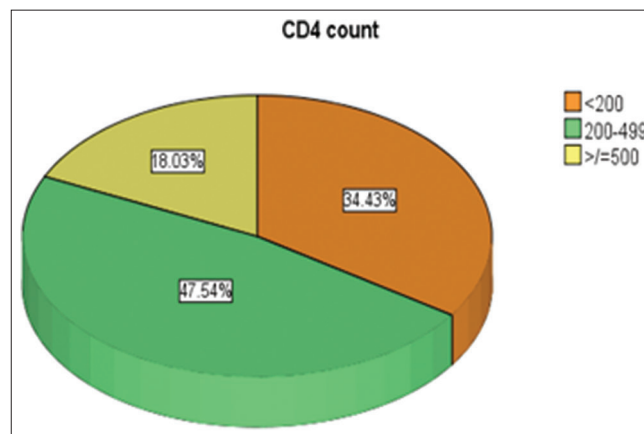


Figure 3: Distribution of HIV-positive patients according to CD4 count

Spectrum of Pulmonary Diseases Noted in Our Study

In our series of 61 patients, about 33 (54%) patients were diagnosed as having pulmonary TB followed by fungal infection (including PJP and cryptococcosis) in 9.8% of the patients, and interstitial lung disease (including BOOP, UIP) in 6.5% patients, while 18% of participants did not reveal any significant abnormality.

Bacterial pneumonia, bronchiolitis obliterans, Kaposi sarcoma, and pulmonary thromboembolism were found in 1.6% of patients each. However, in 4.9% of patients results were inconclusive [Figure 4].

Pulmonary TB

A total of 33 (54%) patients in our study were diagnosed to be suffering from pulmonary TB. The CD4 count in these patients ranged from 74 to 423 cells/mm³. About 12 patients had CD4 count <200 cells/mm³. Different HRCT pattern and their frequency obtained were tabulated in Table 1.

Maximum number (54%) of patients with pulmonary TB were identified to have nodular opacities which were similar to the study conducted by Naseem *et al.*, in which nodules were found in maximum 92% cases.^[9]

Nodules were absent in our five patients. Nodules with cavitations noted in six cases. The centrilobular pattern of distribution was detected in 60.6% of patients, and it was associated with “tree-in-bud” pattern in 55% of cases [Figure 5]. The miliary pattern was evident only in 12.1% of cases [Table 2 and Figure 6].

Lymphadenopathy was noted in 25 (75.7%) cases which is similar to the study conducted by Feng *et al.*, in which the presence of lymphadenopathy was a significant finding (77.2% cases).^[10] Size of the lymph nodes was <1 cm in

14 cases, >1 cm in 11 cases. On contrast administration, seven cases showed peripheral rim enhancement with low-attenuation center suggestive of caseating necrosis due to tubercular infection.

Consolidation was found in 17 (51.5%) cases. Lobar as well as diffusely distributed patches of consolidation were noted among patients.

Cavitation was found in 7 (21.2%) cases. Most of the cavities are located in the upper lung lobes. All the patients having cavitation had CD4 count >200 cells/mm³.

About 11 cases had pleural effusion. Empyema and variable degree lung collapse was noted in three and four cases, respectively.

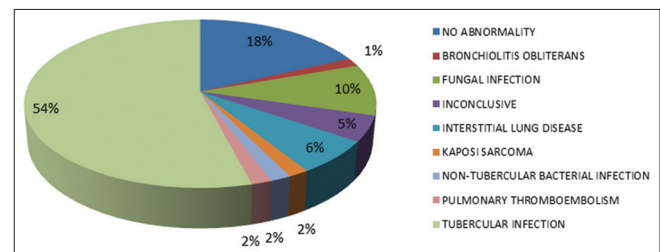


Figure 4: Distribution of HIV-positive patients according to radiological diagnosis

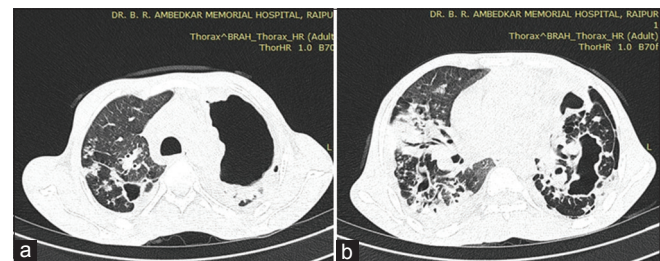


Figure 5: Axial high-resolution computed tomography image at the level of (a) arch of aorta showing multiple centrilobular nodules with clustering and tree-in-bud pattern at some places. Thick-walled cavitory lesion is also seen at the left upper lobe. (b) Airspace consolidation with irregular cavitory lesion noted involving bilateral lower lobes. Case of culture-positive pulmonary tuberculosis

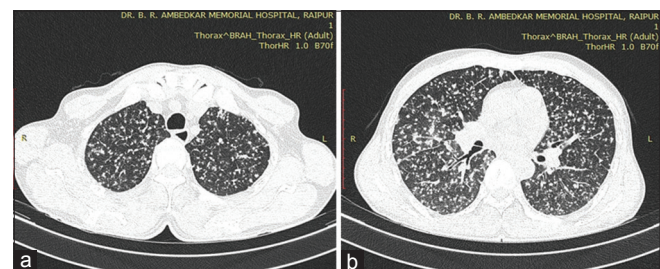


Figure 6: Axial high-resolution computed tomography images (a) through the upper lobes (b) subcarinal level showing miliary nodules diffusely involving bilateral lung fields. Case of miliary tuberculosis

Table 1: HRCT patterns and their frequency in pulmonary tuberculosis cases

HRCT findings	No. of patients (%)
Nodules	28 (84.8)
Lymphadenopathy	
Present	25 (75.7)
<1 cm	14 (56)
>1 cm	11 (44)
Necrotic	7 (28)
Consolidation	17 (51.5)
Cavitation	7 (21.2)
Ground-glass opacity	6 (18.2)
Pleural effusion	11 (33.3)
Empyema	3 (9.1)
Collapse	4 (12.1)
Bronchiectasis	8 (24.2)
Pleural thickening	3 (9.1)
Emphysema	3 (9.1)

HRCT: High-resolution computed tomography

Bronchiectasis was noted in 24.2% of cases of pulmonary TB.

In a 17 year study conducted in Shanghai, China, pulmonary TB was found to be the main cause of bronchiectasis (13.17%).^[11]

Fungal infection

A total of six patients in our study were diagnosed to have fungal infection.

PJP

A total of three patients were diagnosed to be suffering from PJP. The diagnosis was made on the basis of HRCT findings that were later confirmed on bronchoalveolar lavage findings.

In our study, diffuse ground-glass opacity with intralobular and interlobular septal thickening (crazy paving) is seen in all the cases of PJP pneumonia which is fairly correlated with the study of Tasaka *et al.*^[12] Few tiny lung cysts were also noted in all patients [Figure 7]. All the patients were in severe immunocompromised stage with CD4 counts <200 cells/mm³.

Benito *et al.*, reported that HRCT has a high sensitivity for primary cryptococcal pneumonia (100%) and a specificity of 89%.^[13]

Cryptococcosis

Two cases in our study were diagnosed as cryptococcosis. Subpleural nodules were noted in both the patient, one of them showing cavitation [Figure 8]. Both of the cases have CD4 count <100 cells/mm³. Additional magnetic resonance imaging brain studies revealed enlarged perivascular spaces suggesting diagnosis of cryptococcosis.

Aspergillosis

One case was diagnosed as angioinvasive aspergillosis showing characteristic halo sign on HRCT scan, i.e., multiple pulmonary nodules surrounded by ground-glass opacity [Figure 9].

Interstitial lung disease

A total of four cases showed an interstitial pattern of lung disease in our study participants.

UIP

Two cases of UIP was diagnosed in our case study. Diffuse ground-glass opacity with interlobular and intralobular septal thickening was noted predominantly involving bilateral posterior and lower lung zones with honeycombing, and bronchiectasis noted in one patient, centriacinar emphysematous changes along with a large bulla also noted, while in another patient, ground-glass opacity with reticular opacities, consolidation, and bronchiectasis was noted involving posterobasal segment. Their CD4 counts were 403 and 213 cells/mm³, respectively [Figures 10 and 11].

BOOP

Two cases in our study were diagnosed to have BOOP. Patchy consolidation in a subpleural location with bronchiectasis noted. Ground-glass opacity with reticular opacities along with ill-defined nodules was also seen.

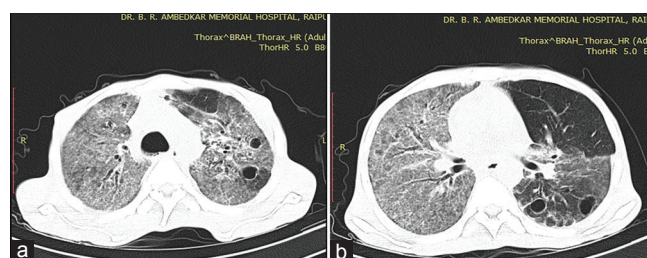


Figure 7: HRCT axial images (a) through the upper lobe (b) subcarinal level showing areas of crazy paving (ground-glass opacity with superimposed interlobular and intralobular septal thickening) and few small cystic lesion. Findings compatible with pneumocystis jiroveci pneumonia

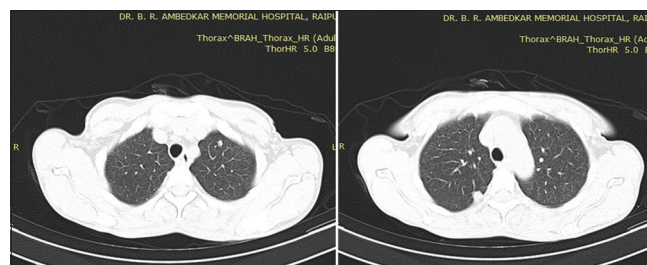


Figure 8: Axial HRCT images through the upper lobes showing subpleural nodules in a case of cryptococcosis

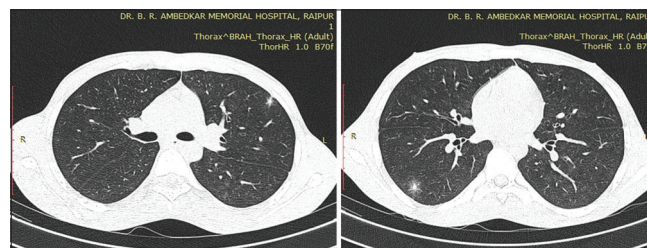


Figure 9: Axial HRCT images showing nodules surrounded by ground-glass opacity (CT-halo sign) in a case of angioinvasive aspergillosis

Table 2: Nodules distribution in TB cases

Distribution of nodules	No. of patients
centrilobular	20
Centrilobular + tree in bud	11
Random + tree in bud	04
Miliary	04

TB: Tuberculosis

Their CD4 counts were 112 and 357 cell/mm³, respectively [Figure 12].

Bacterial pneumonia

One case in our study was diagnosed to be suffering from bacterial pneumonia. HRCT findings include consolidation, bronchiectasis, nodules, and lymphadenopathy [Figure 13].

Magenat *et al.*, and Boisselle *et al.*, reported that focal consolidation was observed in approximately 45–60% of patients with pyogenic infection.^[14,15]

Selwyn *et al.*, found that the combination of focal consolidation of chest radiography and a history of fever for fewer than 7 days was associated with a sensitivity of 48% and a specificity of 94% for the diagnosis of bacterial pneumonia.^[16]

Allen *et al.*, reported that abnormalities may be detected on HRCT in the absence of any CXR findings. These include bronchiectasis and evidence of small airway disease, with

ill-defined centrilobular micronodularity and branching structures or tree-in-bud appearance secondary to mucus impaction in the bronchioles. Mosaic attenuation may also be present due to air trapping.^[7]

Bronchiolitis obliterans

One patient in our study was diagnosed to be suffering from bronchiolitis obliterans. HRCT findings include patchy ground opacities with mosaic attenuation, tubular bronchiectasis diffusely involving bilateral lung fields. Few nodular opacities with a large cystic lesion also noted. His CD4 count was 504 cells/mm³ [Figure 14].

Kaposi sarcoma

One patient in our study was diagnosed to be suffering from Kaposi sarcoma. He presented with complaints

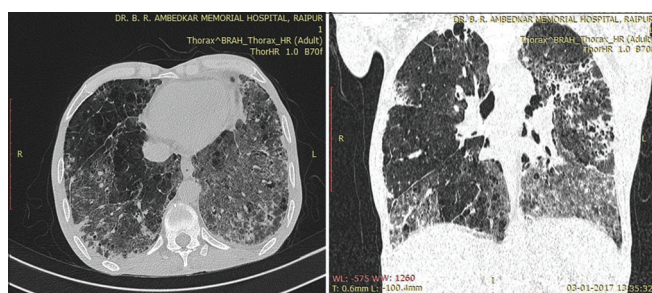


Figure 10: Usual interstitial pneumonia in a 60-year-old male. HRCT axial and coronal reformatted image showing ground-glass opacity with reticular shadowing predominantly involving posterior and lower lung zones. Honeycombing and bronchiectasis can be easily seen

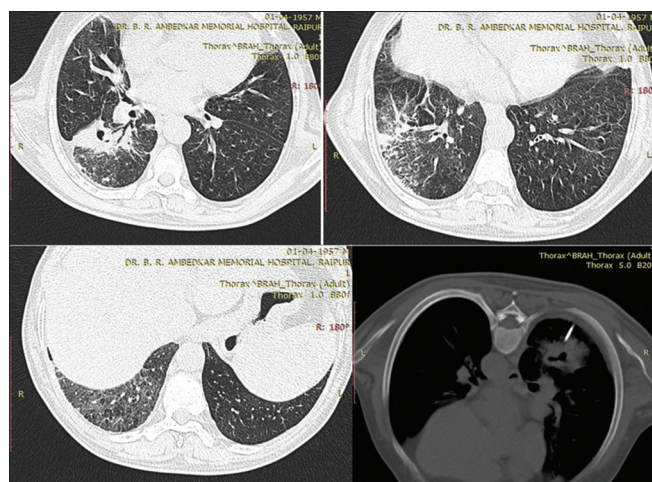


Figure 11: Axial HRCT images through lower lobes showing consolidation and ground-glass opacity with reticular opacities. Few bronchiectatic changes also noted. Last image showing computed tomography-guided biopsy from the lesion. Biopsy demonstrated usual interstitial pneumonia

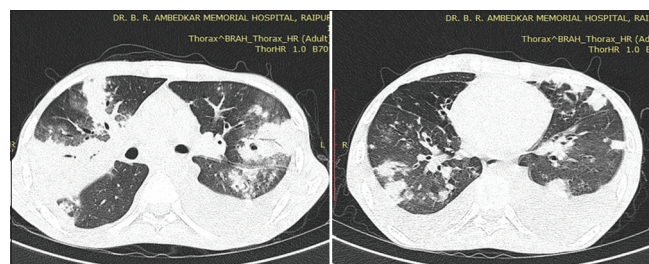


Figure 12: Axial HRCT scan showing the patchy area of airspace consolidation in subpleural in location. Surrounding ground-glass opacity can be clearly seen. Few ill-defined nodules are also noted. Case of bronchiolitis obliterans organizing pneumonia

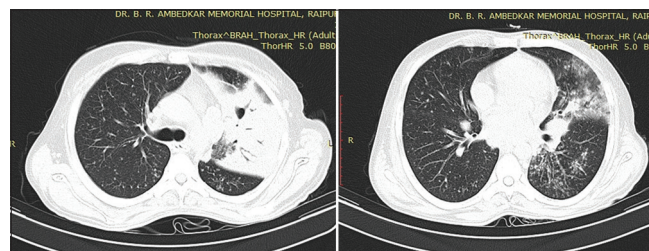


Figure 13: HRCT axial images showing airspace consolidation, focal bronchiectasis, and micronodules in a case of bacterial pneumonia (culture positive for streptococcus)

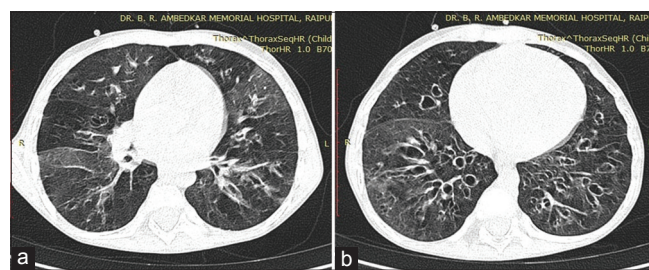


Figure 14: HRCT axial images showing patchy ground-glass opacity with mosaic attenuation (a) and bronchiectatic changes diffusely involving bilateral lower lung likely suggestive of bronchiolitis obliterans (b)

of breathlessness and cough with vascular skin lesions. HRCT findings include peribronchovascular interstitial thickening with flame-shaped nodules in peribronchovascular distribution. Airspace consolidation, ground-glass opacity with reticular opacities and bronchiectatic changes noted involving bilateral lower lobes. Paraseptal emphysema as well as centrilobular emphysematous changes also noted. His CD4 count was 94 cells/mm³ [Figure 15].

Pulmonary thromboembolism

One case in our study was diagnosed to have pulmonary thromboembolism. Thrombus was noted in right main pulmonary artery extending into lobar and segmental branches noted with basal consolidation. Left-sided mild pleural effusion was also seen. His CD4 count was 608 cells/mm³.

Table 3: Diagnostic significance of radiological investigations in diagnosis of pulmonary TB

Radiological diagnosis	Final diagnosis		Total
	Other	Pulmonary TB	
Other			
Count	27	1	28
% within radiological diagnosis	96.4	3.6	100.0
% within final diagnosis	84.4	3.4	45.9
Pulmonary TB			
Count	5	28	33
% within radiological diagnosis	15.2	84.8	100.0
% within final diagnosis	15.6	96.6	54.1
Total			
Count	32	29	61
% within radiological diagnosis	52.5	47.5	100.0
% within final diagnosis	100.0	100.0	100.0

TB: Tuberculosis

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-square	40.123 ^a	1	0.000		
Continuity correction ^b	36.930	1	0.000		
Likelihood ratio	47.716	1	0.000		
Fisher's exact test				0.000	0.000
No. of cases ^b	61				

Parameter	Value (%)	95% Confidence interval (%)
Sensitivity	96.5	80.4–99.8
Specificity	84.3	66.4–94.1
PPV	84.8	67.3–94.3
NPV	96.4	79.7–99.8

PPV: Positive predictive value, NPV: Negative predictive value

The sensitivity and specificity to detect pulmonary TB by HRCT were found to be 96.5% and 84.3%, respectively [Table 3].

We compared the CD4 counts with different outcomes (i.e., death, deterioration, and improvement on follow-up). The mean CD4 count was found to be lower in patients with death, poor treatment responders, and the highest with clinical symptomatic improvement; however, the difference failed to reach statistical significance ($P < 0.0001$) [Figure 16 and Table 4].

Prognostic significance of CD4 count was demonstrated using ROC curves in which 66.9% area comes under the curve with a sensitivity and specificity 72.5% and 62.5%, respectively [Table 5].

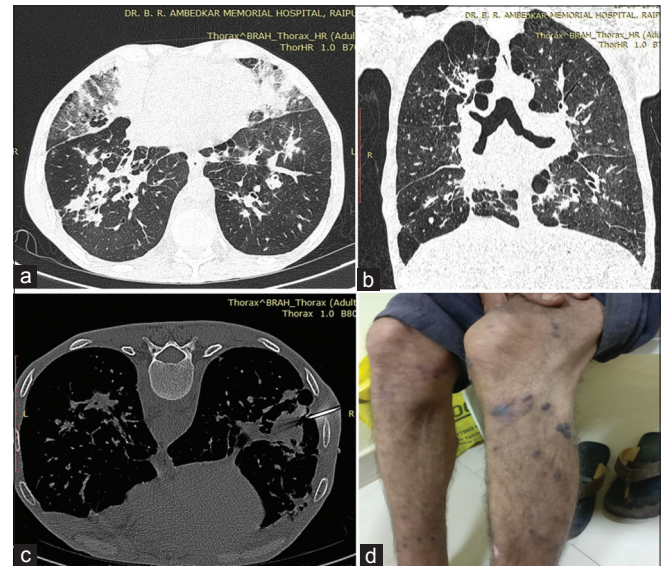


Figure 15: (a) Axial HRCT image and (b) coronal reformatted images showing thickening of peribronchovascular bundles with characteristic flame-shaped nodules in peribronchovascular distribution. Consolidation with ground-glass opacity and reticular opacities noted in the bilateral middle lobe. (c) Image showing computed tomography-guided biopsy from the lesion. Biopsy demonstrated Kaposi sarcoma. (d). Clinical image showing vascular skin lesions.

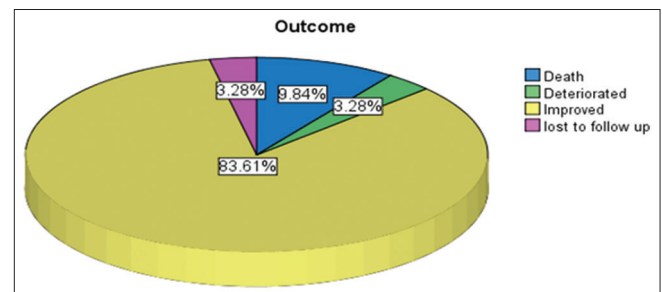


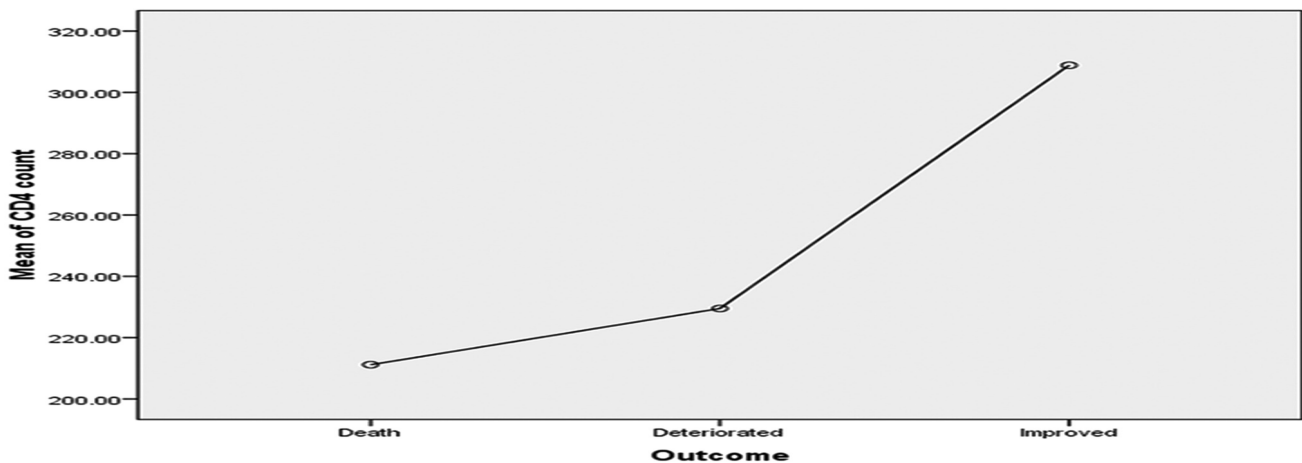
Figure 16: Distribution of outcomes among symptomatic adult HIV-positive patients

Table 4: Comparison of CD4 count in different outcomes in study participants

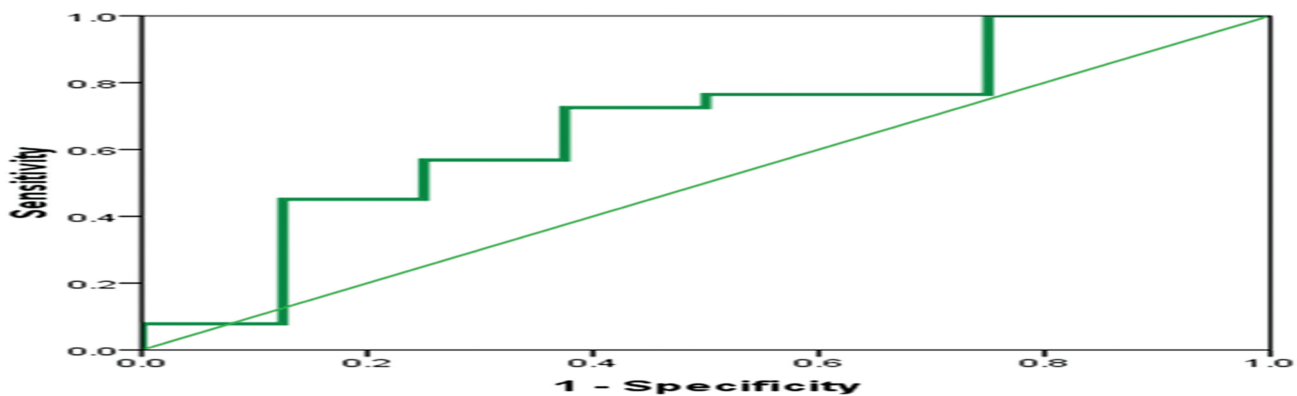
CD4 count	N	Mean	Std. deviation	Std. error	95% Confidence interval for mean		Minimum	Maximum
					Lower bound	Upper bound		
Death	6	2.1117E2	208.54392	85.13770	-7.6868	430.0201	28.00	608.00
Deteriorated	2	2.2950E2	123.74369	87.50000	-882.2929	1341.2929	142.00	317.00
Improved	5	3.0884E2	170.116	23.8211	260.9970	356.689		
	1	2	94	4		3	74.00	710.00
Total	59	2.9622E2	173.21444	22.55060	251.0804	341.3603	28.00	710.00

ANOVA**CD4 count**

	Sum of squares	df	Mean square	F	Sig.
Between-groups	60434.057	2	30217.029	1.007	0.372
Within groups	1679754.078	56	29995.609		
Total	1740188.136	58			

**Table 5: Prognostic significance of CD4 count****Area under the curve**

Test result variable (s):CD4 count			Asymptotic 95% confidence interval		Cutoff	Sensitivity %	Specificity %
Area	Std. Error ^a	Asymptotic Sig. ^b	Lower bound	Upper bound			
0.669	0.108	0.127	0.458	0.880	193	72.5	62.5



CONCLUSION

Pulmonary TB was the most common pulmonary manifestation in HIV patients followed by fungal infection (including PJP and cryptococcosis) and interstitial lung disease (including BOOP and UIP). The incidence of all these disease manifestations fairly correlates with the decline of CD4 counts. Early and proper diagnosis of these pulmonary complications in patients with HIV infection will help clinicians develop a focussed therapeutic approach to patient management.

HRCT is a highly sensitive tool for detecting lung parenchymal and interstitial lesions and allows better characterization of the lesions. Conventional radiography has low sensitivity and specificity and at many times does not lead to a conclusive diagnosis specially in complex situations where multiple infection is commonly seen. The lesions which are not detected or are equivocal on plain radiographs are identified and can be categorized as being active or inactive and thus helps to plan timely management, thereby reducing the morbidity and mortality from respiratory diseases in HIV patients. Hence, we recommend HRCT in the diagnosis, treatment, and follow-up of these patients with pulmonary manifestations. Its noninvasive nature and relatively quicker time of scan make it a suitable choice in these patients.

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