# High-resolution Computed Tomography Lung Spectrum in Symptomatic Adult HIV-positive Patients in Correlation with CD-4 Count

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#### Abstract

**Context:** Pulmonary disease accounts for 30–40% of the acute hospitalizations of HIV-positive patients. The CD4 count, an indicator of the severity of immune compromise, is of paramount importance for rendering an appropriate differential diagnosis. High-resolution computed tomography (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.

**Aims:** The aims of this study were as follows: (1) To identify the radiological appearance/pattern of HIV-associated infections. (2) To correlate the radiological findings with CD4 count.

**Settings and Design:** This was a cross-sectional study using sample size of 100 HIV-infected patients conducted at the Department of Radiodiagnosis and Imaging, Gandhi Medical College and Hamidia Hospital, Bhopal.

**Materials and Methods:** A total of 100 adult HIV-infected patients were scanned with HRCT chest and findings were documented and correlated with their CD4+ counts.

Statistical Analysis Used: Data analysis was done using SPSS 21.0. Two-tailed P < 0.05 was considered statistically significant.

**Results:** TB (70%) was the most common infection followed by bacterial pneumonia (14%) and *Pneumocystis jiroveci* pneumonia (6%). Tuberculosis was found in 29% of advance CD4 count patients and 27% of severe CD4 count patients. Consolidation, airspace nodules, miliary nodules, diffuse ground-glass opacity, and pleural effusion showed significant correlation with CD4 counts.

**Conclusions:** Incidence of all these manifestations fairly correlates with the decline of CD4 counts. Early and proper diagnosis of these pulmonary complications in patients with HIV infection and lower CD4 counts will help clinicians to develop a focused therapeutic approach in their management.

**Key words:** AIDS, CD4 counts, Fungal ball, Ground-glass opacity, High-resolution computed tomography, HIV infected, Tuberculosis

#### INTRODUCTION

From the first descriptions of HIV/AIDS, the lung has been most frequently affected by the disease. Most patients develop a pulmonary complication during a history of HIV

Access this article online				
IJSS	Month of Submission : 11-2018 Month of Peer Review : 12-2018 Month of Acceptance : 12-2018 Month of Publishing : 01-2019			
www.ijss-sn.com	Month of Publishing : 01-2019			

infection, mainly of infectious etiology. The first published reports of AIDS appeared in 1981 when five homosexual males in Los Angeles (CA, USA) were diagnosed with *Pneumocystis carinii* (currently, *Pneumocystis jiroveci*) pneumonia. Since then, HIV infection has become a pandemic and remains one of the most important global health problems of the 21<sup>st</sup> century.

The prevalence of patients with HIV infection continues to increase worldwide. Pulmonary disease accounts for 30–40% of the acute hospitalizations of HIV-positive patients. HIV infection causes alteration in several lines of host defenses in the lung and respiratory tract that

**Corresponding Author:** Mayank Kumar Ujjaliya, B,197 Veena Nagar,Sukhaliya, indore,Madhyapradesh. Pin -452010. Mobile: 9098394923. E-mail: mayankujjaliya.ujjaliya@gmail.com. Dr Sudeept Dwivedi, Postgraduate in department of radiodiagnosis, Gandhi medical college, Bhopal, Madhya Pradesh,India. Phone: 8319293819. E-mail: drsudeept@gmail.com contributes to an increased risk for lung complications. Many well-described infectious diseases, cancers, and other pulmonary diseases occur with increased frequency in this population.

Worldwide, TB is the major cause of mortality in persons with HIV infection and the World Health Organization (WHO) estimates that TB is the cause of death for 13% of persons who die with HIV/AIDS. The CD4 count, an indicator of the severity of immune compromise, is of paramount importance for rendering an appropriate differential diagnosis. Although all HIV-infected patients are at increased risk of bacterial pneumonia and tuberculosis (TB) compared with the general population, opportunistic infections are uncommon in patients with a CD4 count >200 cells/mm<sup>3</sup>. Patients with AIDS with a CD4 count <200 cells/mm<sup>3</sup> are at increased risk for certain infectious pathogens such as P. carinii pneumonia (PCP) and atypical mycobacteria. Moreover, some infectious pathogens, such as cytomegalovirus and disseminated fungal and mycobacterial infections, are uncommon in HIV-infected population until CD4 counts fall <100 cells/mm<sup>3</sup>. Finally, the change in imaging manifestations of disease and the clinical response to treatment provide important diagnostic information.

High-resolution computed tomography (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. Hence, my study is intended to document these radiological findings and correlate them with patient's CD4 counts.

## **MATERIALS AND METHODS**

This was hospital-based cross-sectional study done at the Department of Radiodiagnosis, Gandhi Medical College and Hamidia Hospital, Bhopal, using purposive sampling and a sample size of 100 HIV-infected patients with documented CD4+ counts, referred to our department for chest assessment.

All subjects were enrolled with detailed oral and written consent.

This study was approved by ethical and scientific committee of our institute.

#### **Inclusion Criteria**

On the basis of clinical presentation and plain radiography, all HIV-positive adult patients of age more than 18 years, who presented with lung disease, were included in the study.

#### **Exclusion Criteria**

The following criteria were excluded from the study:

- 1. <18 years age
- 2. Pregnant HIV-positive females.

#### Instrumentation and Technique

All examinations are going to be performed on CT/e Wipro 16 slice GE computed tomography machine.

#### *Technique of scanning* Patient preparation

The procedure and objectives of performing the highresolution CT scan were explained to patient and written consent of patient was taken. Prior fasting was not advocated as the procedure did not warrant the need for contrast injection. The patient was explained and demonstrated the procedure of breath holding during the acquisition of HRCT scans.

#### HRCT protocol Patient position

The patient was kept on gantry table in supine position and scans were taken cephalocaudal in the axial axis. In most instances, scans taken with patients in supine position were adequate. The tomogram or scanogram was first taken, and then, scanning of whole lung is done from apex to the base. Using the following protocol, scans were performed on CT/e Wipro GE scanner.

Collimation = 1 mm KVp = 120-140mA = 250

#### **Reconstruction Algorithm**

To reduce image smoothening and increase spatial resolution, high spatial frequency algorithm was used. It makes structures appear sharper.

Grouping into CD4+ classes is done according to the WHO's classification of CD4+ immunological profile in adult HIV-infected patients,

- CD4+ counts >500/µL categorized into none or not significant class.
- 2. 350-499 as mild.

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- 3. 200–349 as advanced.
- 4. <200 as severe category.

Complete evaluation of all patients was done in the following format:

- Clinical history and examination.
  - Laboratory investigations which include:
    - HIV status, CD4 counts,
    - Routine blood examination,

- Sputum examinations, pleural fluid analysis, and other available investigations.
- Chest X-ray.

#### **Statistical Analysis**

Data analysis was done using SPSS 21.0. Variables were expressed as percentages and comparison was by Chisquare analysis. Two-tailed P < 0.05 was considered statistically significant.

Graph 1 reveals frequency distribution of HRCT findings among symptomatic adult HIV-positive patients. Airspace nodules were found positive on HRCT in maximum 65% HIV patients followed by consolidation in 53% of patients. Pleural effusion and lymphadenopathy were also more frequently present in 44% and 41% of patients, respectively.

## RESULTS

In our study, maximum number of patients was in the age group of 20–40 years. There were 90 patients in the age group of 20–40 years. Of 100 patients included in our study, 65 (65%) were male and 35 (35%) were female. Hence, here, male-to-female ratio was 1.8:1.

#### **Pulmonary Diseases Noted in our Study**

- In our study of 100 patients, number of patients diagnosed as having pulmonary TB 70% of cases.
- Bacterial pneumonia 14% of cases.
- *P. jiroveci* pneumonia (PJP) 6% of patients, while 10% of the study did not reveal any significant abnormality.

These diagnoses were made on the basis of imaging findings along with clinical complaints of the patients and laboratory findings.



Graph 1: Frequency distribution of high-resolution computed tomography findings among symptomatic adult HIV-positive patients

#### Table 1: Association of diagnosis with CD4 count among symptomatic adult HIV-positive patients

Diagnosis	CD4 count					
	Not significant (>500) (%)	Mild (350–499) (%)	Advance (200-349) (%)	Severe (<200) (%)	Total	
Normal	4 (40)	6 (60)	0 (0.0)	0 (0.0)	10	
ТВ	0 (0.0)	14 (20)	29 (41.4)	27 (38.6)	70	
Bacterial pneumonia	0 (0.0)	4 (28.6)	7 (50.0)	3 (21.4)	14	
PCP	0 (0.0)	0 (0.0)	0 (0.0)	6 (100)	6	
Chi-square value	61.905					
Significance "P" value	0.001 (HS)					

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#### Pulmonary TB

In our study, 70 patients of 100 patients were diagnosed pulmonary TB. The CD4 count in these patients varied from 54 to 460 cells/mm<sup>3</sup> with a mean count of 172 cells/mm<sup>3</sup>. The number of patients having CD4 counts <200 cells/mm<sup>3</sup> was 27.

Maximum number (47/70) of patients with pulmonary TB were identified to have nodular opacities. The size of the nodules in all the cases was <1 cm with majority of them being 1–5 mm in size. In about 35 patients, nodules were ill defined, that is, in 74.4% of patients [Figure 1].

Well-defined nodules were noted in six patients only [Figure 2].

- Well-defined nodules with cavitation were noted in six patients.
- Centrilobular pattern of distribution was noted in 71.4% of cases and it was associated with tree in bud opacity in 12.8% of cases.



Figure 1: Pulmonary tuberculosis: Scan at carinal level showing consolidation with cavitation in left upper lobe with scattered nodular opacities in bilateral upper lobes.

• Miliary pattern was noted 21.4% of the cases [Figure 3].

Thick-walled cavitation was found in 24 patients and thinwalled cavitation was found in six patients [Figure 4]. The location of these cavities was as 16 cases in the right upper lobe, six cases in the right lower lobe, five cases in the left upper lobe, and three cases in the left lower lobe.

About 53.4% of the patients who had cavitation were found to have CD4 count >200 cells/mm<sup>3</sup>.

Aspergilloma or fungal ball noted in four cases of tubercular cavity [Figure 5] in which three cases in the right upper lobe and one case in the left upper lobe, CD4 count of all these patients belongs to severe group.

Collapse was noted in 11(15.7%) patients of tuberculosis, out of which 7 in right upper lobe and 4 in left upper lobe.

Lymphadenopathy was noted in 39/70 (55.7%) cases;

- The hilar region in 12 patients,
- Mediastinal in 18 patients,





Figure 2: Pulmonary tuberculosis: Scan at subcarinal level shows multiple air space nodules with irregular septal thickening involving bilateral upper lobes

Figure 3: Miliary tuberculosis: Scan at hilar level showing diffuse subcentimetric nodules in bilateral lungs fields



Figure 4: Pulmonary tuberculosis: Scan at the level of lung apices showing bilateral apical bullae with adjacent patchy consolidation in left upper lobe.

- Both hilar and mediastinal lymphadenopathy in nine patients,
- Calcification in lymph nodes was noted in five patients.

Pleural effusion was noted in 33/70, that is, 47.1% of cases. Bilateral pleural effusion was noted in nine patients while 24 patients had unilateral pleural effusion. Among these patients with unilateral pleural effusion, 16 had right-sided pleural effusion while 8 had left-sided pleural effusion [Figure 6].

In 20 of 70 patients with pulmonary TB, bronchiectasis was noted. Bronchial wall thickening was seen in 12 patients with bronchiectasis.

Fibrotic opacities were seen in 15 patients who suggest old healed infective process in addition to the active pathology.

Bulla was seen in 11 (15.7%) cases of TB.

#### Bacterial infection

In our study, a total of 14 patients were diagnosed to be suffering from bacterial infection. The CD4 count in these



Figure 5: Pulmonary tuberculosis: Scan at the level of lung apices showing irregular cavity in right upper lobe with dependent soft tissue/fungal ball. Bulla in the apicoposterior segment of left upper lobe



Figure 6: Pulmonary tuberculosis: Scan at aortic root showing moderate right sided pleural effusion with passive collapse of right lower lobe

patients varied from 108 to 410 cells/mm<sup>3</sup>, with a mean count of 212 cells/mm<sup>3</sup>. The most common HRCT finding in bacterial infection was lobar consolidation noted in 8 (57.1%) patients followed by focal consolidation, noted in 7 (50%) cases and bronchiectasis was noted in 6 (42.8%) cases [Figures 7 and 8].

## PJP

A total of six patients in our study were diagnosed as PJP. The most common HRCT finding was diffuse groundglass opacities seen in 4 (66.6%) cases. Classic appearance of crazy paving and GGO was seen in two patients [Figure 9]. Few tiny cystic lesions were also noted in two cases in bilateral upper lobes. All of these patients were in severe immunocompromised stage with CD4 counts <200 cells/mm<sup>3</sup>, ranging from 20 to 60 cells/mm<sup>3</sup> with a mean count of 32 cells/mm<sup>3</sup>. Randomly distributed nodules measured 1–5 mm in size, >5 nodules were noted in five cases.



Figure 7: Bacterial pneumonia: Scan at atrial level showing lobar consolidation involving right lower lobe with characterstic absence of air bronchograms



Figure 8: Bacterial pneumonia: Scan at tracheal level showing focal consolidation involving anterior segment of left upper lobe and patchy consolidation in bilateral upper lobes



Figure 9: Pneumocystitis Pneumonia: Scan at cardiac ventricles level showing bilateral lower lobes ground glass opacities giving Crazy Paving appearance

## DISCUSSION

The disease activity, pattern, degree of involvement, and associated complications were better evaluated with the help of HRCT examination.

According to NACO, HIV estimation 2015:[1]

Total 21.17 lakhs peoples are living with HIV in india in 2015. Incidence of HIV is estimated to 86,300 which is 66% reduction since 2000. AIDS-related death amounts to 67,600, which is 54% reduction since 2007. 10,400 new HIV infections are estimated in children and TB-related deaths among PLHIV amounts to 31,000.

As per the recently released, NACO annual report 2015–2016,<sup>[1]</sup> HIV prevalence in India is estimated 0.26% (0.22–0.32%) in 2015. In 2015, adult HIV prevalence is estimated 0.30% among males and 0.22% among females.

Age range of cases varied from 18 to 50 years with the maximum number of cases in the age group of 21–30 years (45%) followed by 31–40 years (45%). More than half of the cases (90%) belonged to the age group of 20–40 years. Further, 35% of the cases included in the study were female and 65% were male. This age and sex range nearly corresponds to the data provided by NACO 2015 report.

Of 100 cases in the study, we found among 4% of patient CD4 count were not significant. Among 24% of HIV patients CD4 count were mild. Advance and severe CD4 count were seen in 36% of patients each.

According to the WHO 2014 report, the risk of developing TB is estimated to be between 26 and 31 times greater in

people living with HIV than among those without HIV infection. In 2014, there were 9.6 million new cases of TB, of which 1.2 million were among people living with HIV.<sup>[2]</sup>

#### **Pulmonary TB**

TB (70/100) was found to be the most common disease affecting HIV patients in our study.

The WHO reported that in 2014, an estimated 1.2 million (12%) of the 9.6 million people who developed TB worldwide were HIV positive. The African Region accounted for 74% of the estimated number of HIV-positive incident TB cases.<sup>[2]</sup>

TB disease is the most common opportunistic infection among HIV-infected individuals. Further, it is also known that TB is a major public health problem in India accounts for 20–25% of deaths among PLHIV. It is known that nationally about 5% of TB patients registered under the Revised National TB Control Programme also have HIV infection. In high prevalent states and districts, positivity among TB patients is more than 10% and is as high as 40% in selected districts.<sup>[3]</sup> Thus, while the country is dealing effectively with HIV burden, TB-associated HIV epidemic is posing a great challenge.

To assess the morphological changes of lung parenchyma, CT is considered as the gold standard.

In our study, 67.1% of patients demonstrated the presence of nodular opacities followed by consolidation (65.7%) which is similar to the study conducted by Naseem *et al.*<sup>[4]</sup>

In our study, lymphadenopathy was seen in 55.7% cases, which was near similar to study done by Almeida *et al.* 

TB lymph nodes are typically markedly enlarged and of low attenuation on CT. Patients with lower CD4 count have an increased incidence of miliary TB, with diffuse, randomly distributed nodules on CT, as found in the study of Keiper *et al.*<sup>[6]</sup>

Hilar and mediastinal lymph node involvement is commonly seen in HIV positive patients on HRCT.

In pulmonary TB, pleural effusion is a common complication. Effusion is mostly exudative in nature. Unilateral effusion is more common than bilateral. In our study, pleural effusion was found in 47.1% which is nearly similar to a study done by Almeida *et al.*,<sup>[5]</sup> in which 64.4% of cases had pleural effusion.

Bronchiectasis is generally defined as localized, irreversible bronchial dilatation, often associated with thickening of

the bronchial wall. A bronchus is considered to be dilated if the bronchoarterial ratio exceeds 1.

In a 17 years study conducted in Shanghai, China, pulmonary TB was found to be main cause of bronchiectasis (13.17%). Bronchiectasis is seen in 28.5% of cases in our study.

Emphysematous bulla noted in 12 (17.1%) cases in our study. Emily Clausen *et al.*<sup>[7]</sup> noted that emphysema was the most common finding (26.4%) in their study.

### **TB** with Fungal Ball

Cavitation was seen in 30 tubercular cases, of which four cases show aspergilloma or fungal ball in the cavity. Guazzelli *et al.*<sup>[8]</sup> reported six cases of fungal ball in patients with AIDS. In this group, all patients had hemoptysis and TB as the underlying lung disease.

#### **Bacterial Infection**

Bacterial infection was found in about 14% of cases. Our study finding is fairly correlating with the study of Hirschtick *et al.*<sup>[9]</sup>

Lobar consolidation was the most common HRCT finding in bacterial infection seen in 57.1% of patients followed by focal consolidation (50%) and bronchiectasis (42.8%). These findings are consistent with the study of Aviram and Boiselle,<sup>[10]</sup> in which focal consolidation was observed in approximately 45–60% of patients with pyogenic infection.

Allen *et al.*<sup>[11]</sup> 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.

### PJP

A total of six patients in our study were diagnosed to be suffering from PJP. The diagnosis was established on the basis of HRCT findings and the clinical profile of the patients along with the findings of bronchoalveolar lavage.

In our study, diffuse ground-glass opacity is seen in all the cases of PCP pneumonia which is fairly correlated with the study of Tasaka *et al.*,<sup>[12]</sup> and the study of Singh *et al.*<sup>[13]</sup>

Pneumocystis pneumonia typically presents with extensive ground-glass opacity that may be patchy or diffuse with a central, perihilar, and upper lobe predominance. Accompanying findings may be the thickening of the interlobular septae and rarely the "crazy paving" pattern. Less common manifestations may include the upper lobe lung cysts and areas of consolidation. Differentiating findings from hypersensitivity pneumonitis may be the presence of upper lobe cysts and the associated "crazy paving" pattern. History of immunosuppression, and especially AIDS, favors the diagnosis of pneumocystis pneumonia.

HRCT is very sensitive, the hallmark being ground-glass opacity which is seen in over 90% of the cases and often has a geographic or mosaic distribution, reflecting accumulation of intra-alveolar fibrin, debris, and organisms.

## CONCLUSION

Pulmonary tuberculosis was the most common pulmonary manifestation in HIV patients followed by bacterial pneumonia and pneumocystis jiroveci pneumonia and incidence of all these manifestations fairly correlate with the decline of CD4 counts. Early and proper diagnosis of these pulmonary complications in patients with HIV infection and lower CD4 counts will help clinicians to develop a focussed therapeutic approach in their management.

Conventional chest radiography does not rule out the diagnosis of tuberculosis and also less sensitive for other pneumonia, particularly in HIV/AIDS patients and therefore CT scan should be performed in the patients with clinical suspicion of this diseases.

Our study data support the fact that HRCT can be a lot better option than conventional radiographs in complex situations where radiographs cannot differentiate between active disease from old infective/fibrotic changes.

So we recommend that HRCT be used in conjunction with chest radiographs in diagnosis, treatment and follow up of HIV/AIDS patients with pulmonary manifestations. Its non-invasive nature and relatively quicker time of scan makes it a suitable choice in these patients

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How to cite this article: Ujjaliya MK, Dwivedi S. High-resolution Computed Tomography Lung Spectrum in Symptomatic Adult HIV-positive Patients in Correlation with CD-4 Count. Int J Sci Stud 2019;6(10):5-12.

Source of Support: Nil, Conflict of Interest: None declared.