



ROLE OF HRCT THORAX IN DETECTION AND CHARACTERIZATION OF PULMONARY PATHOLOGIES IN HIV PATIENTS WITH LOW CD4 COUNTS- A PROSPECTIVE OBSERVATIONAL STUDY

Radiodiagnosis

Sharma Ashok Kumar

MBBS; MD Radiodiagnosis. Senior Resident Dept. of Radiodiagnosis and Imaging, B.J. Medical College and Sassoon General Hospitals, Pune-1, India.

Pawar Shephali Shrikant*

MBBS; MD Radiodiagnosis. Professor and Head of Department, Dept. of Radiodiagnosis and Imaging, B.J. Medical College and Sassoon General Hospitals, Pune-1, India.
*Corresponding Author

ABSTRACT

Background: Human immunodeficiency virus (HIV) weakens the host immune system and makes them prone to various opportunistic infections and malignancies. Etiology and patterns of pulmonary pathologies in HIV patients depend on CD4 counts, which is a measure of immunosuppression.

Aims: This study was conducted to assess the pattern of pulmonary infection in HIV patients with low CD4 counts using conventional chest X-ray (CXR) and High-Resolution Computed Tomography (HRCT) thorax and further to compare the findings of both CXR and HRCT.

Subjects and Methods: The study was carried out over a period of 18 months including 50 consenting HIV patients with CD4 count less than 500 cells/ μ l having clinical symptoms like cough and fever. All the participants were sent for chest radiograph as well as HRCT thorax plain and contrast.

Statistical analysis used: All data were analyzed by Chi-Square test and One-way ANOVA with SPSS 16.0 software.

Results: The mean CD4 count was 232.5 ± 132 cells/ μ l. The diagnosis based on abnormal HRCT included cases of Pulmonary Tuberculosis (36%), Bronchopneumonia (10%), Viral pneumonia (4%), metastasis from Hepatocellular carcinoma (4%), Angioinvasive aspergillosis (2%), metastasis from NHL (2%), lung adenocarcinoma (2%), cardiomyopathy (2%) and chronic kidney diseases (2%) in HIV patients. There was no significant correlation with CD4 count and pulmonary pathologies. However, all patients with Miliary TB, PJP, aspergillosis and CMV had CD4 count less than 200 cells/ μ l.

Conclusions: We concluded that HRCT thorax is a highly sensitive tool for detecting HIV associated opportunistic infections as well as lesions and allows their better characterization.

KEYWORDS

HIV, Low CD4 count, HRCT thorax, Opportunistic infections.

INTRODUCTION

According to UNAIDS report, 2017; Human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) infection has emerged as a universal pandemic and more than 25 million population have died of AIDS since 1981. India has the third largest HIV epidemic in the world and approximately 2.1 million people having HIV with prevalence rate approximately 0.3%. [1] There is acquired, irreversible immunodeficiency in AIDS patients due to decreased CD4 count results in increased incidence of numerous opportunistic infections (OIs), malignant cancers and dysfunction of various body systems. [2] Diverse disease spectrum is seen at a various range of CD4 cell below 500 cells/ μ l and the most often involved organ in the immunosuppressed HIV host is the lung. [3]

Chest X-ray (CXR) is frequently used as a part of screening of lung pathologies in HIV positive patients. Conventional CXR is of low cost, effective and easily available but it lacks selectivity and specificity. In 1982, Todo et al. reported the importance of High-Resolution Computed Tomography (HRCT) for evaluation of various pulmonary pathologies. HRCT can visualize secondary pulmonary lobule and alveoli which add in assessment of the pulmonary pathologies. [4]

Hence, the current study was undertaken to evaluate the effectiveness of HRCT thorax in the early detection and characterization of pulmonary abnormalities in HIV patients with low CD4 counts. We further attempted the comparison of HRCT with CXR and correlation of CD4 levels with pulmonary pathologies.

SUBJECTS AND METHODS

This hospital based prospective observational study was conducted in Department of Radiodiagnosis, BJGMC & SGH, Pune after getting approval from Institutional Ethics Committee (BJGMC/IEC/Pharmac/D-1216190-190). A total number of 50 consenting HIV patients with low CD4 counts (<500 cells/ μ l) who were presented with fever, cough and dyspnoea were studied over a period of 18 months (Dec 2016-June 2018).

Inclusion criteria was HIV positive adult (>18 years) patients with CD4 count less than 500 cells/ μ l of both sexes who suspected with lung disease on the basis of clinical profile. Exclusion criteria were patients who have suspected lung disease but HIV negative or HIV patients

with CD4 counts more than 500 cells/ μ l, pregnant patients, paediatric (0-18 years), severely deranged renal status, contrast sensitive and all patients who do not give consent to be part of the study.

Imaging Technique

X ray machines including digital radiography (Prognosys Medical System Prorad 3NC DR System) and Computed radiography (Alfa Healthcare DX-D 100 CR System) were used for chest radiograph. Chest radiography comprised of standing posteroanterior (PA) and lateral radiographs at 120 kVp.

The HRCT thorax were performed using Siemens Somatom definition AST 65983 mmwp-70527 (64x2) slice Multidetector CT scan machine with CPT software. The scanning parameters were 1 mm collimation at 1 cm intervals, 120kVp and 250mAS and scan time 1 to 2sec. The CT images were taken at standard window levels and widths for lung parenchyma (level=-550 to -700 HU, width = 1000-1650 HU) and mediastinum (level = 30-50 HU, width = 350-400 HU).

Image Interpretation

The CXR and HRCT scans were examined for the presence of consolidation, ground-glass opacities, nodular opacities, linear/reticular opacities, lymph nodes, fibro bronchiectatic changes, mass, pleural effusion, cardiomegaly and pericardial effusion. Nodules were classified by distribution, size, pattern (Tree in Bud, Centrilobular, Clustered, Random), and presence of cavitation or surrounding halos.

On CXR, typical Pulmonary TB (PTB) was defined as upper lobe fibrosis, bilateral infiltrates, consolidation and cavitation, while atypical cases were diagnosed when there is less cavitation, enlarged mediastinal lymph nodes, lower lobe and diffuse interstitial infiltrates. Miliary TB was diagnosed when bilateral widespread discrete 1-2mm lung nodules were seen.

Statistical analysis

Chi-Square test and One-way ANOVA was done to analyses data using SPSS 16.0 software. Data are presented as Mean $\pm$ Standard deviation and as Percentage. The level of significance was set at $P < 0.05$.

RESULTS

Total 50 patients were included in the study. Around 78% patients were 21-50-year-old, 14% were more than 50-year-old and only 8% patients were less than 20-year-old. Among all the patients 62% were males and 38% were females with male and female ratio of 1.6:1. While taking clinical history, 98% HIV patients were presented with cough followed by fever (92%), weakness (22%) and weight loss (20%). In current study, the mean CD4 counts were 232.5 ± 132 cells/ μ l, $66\% \leq 300$ cells/ μ l and $34\% > 300$ cells/ μ l. The patient with Miliary TB, Pneumocystis jirovecii pneumonia (PJP) and cytomegalovirus (CMV) had CD4 count less than 200 cells/ μ l (Table 2).

Chest radiograph findings

On chest radiograph, lungs of maximum (32%) patients had alveolar or interstitial infiltrates tailed by nodules (22%), lymphadenopathy and pleural effusion (12% each) and Ground glass opacities (GGO) (10%). A small number of patients were seen with bronchiectasis, cardiomegaly and mass (8% each). Furthermore, 21 (42%) subjects had normal chest radiographs.

On the basis of radiographic findings PTB were diagnosed in 13 (26%) cases including primary TB (5, 10%), reactivation TB (3, 6%), old TB (3, 6%) and miliary TB (2, 4%). Other HIV-positive patients were diagnosed with bacterial pneumonia 4 (8%), PJP/Viral pneumonia 3 (6%) and PJP 2 (4%), metastasis 3 (6%), Pleural effusion 2 (4%), primary lung malignancy 1 (2%) and 1(2%) isolated cardiomegaly. On X-ray PJP and Viral pneumonia both shows diffuse GGO, however nodules were more common in viral and perihilar GGO were more common in PJP.

Pulmonary TB patients, 83.3% (15/18) had atypical patterns. Majority of 55.5% (10/18) patients showed infiltrates at the middle and/or lower zones, diffuse, bilateral or unilateral side of the lungs, followed by 33.3% (6/18) had mediastinal lymphadenopathy, 22.2% (4/18) revealed pleural effusion and 11.1% (2/18) presented with miliary TB.

HRCT findings

In HRCT, commonest lesion visible in lungs was nodules (38%), followed by GGO (28%), lymphadenopathy (22%) and fibro-bronchiectasis (20%), then pleural effusion (16%) consolidation (14%) and pericardial effusion (10%) (Table 1).

From 50 patients, 18 (36%) patients were diagnosed with PTB including 7 (14%) primary TB, 5 (10%) reactivation TB, 3(6%) Old TB, and 3 (6%) miliary TB. One patient with primary TB presented with empyema and one old TB with fungal ball. Among TB patients, 66.7% (11/18) patients had airspace nodules followed by lymphadenopathy 44.4% (8/18, $\frac{3}{4}$ patients shows necrosis), fibro-bronchiectasis 38.8% (7/18), pleural effusion 22.2% (4/18), ground-glass opacity 22.2% (4/18), mild cardiomegaly with pericardial effusion 16.7% (3/18) in all miliary TB, consolidation 11.1% (2/18), emphysema 11.1% (2/18) (Figure 1). We found that majority of cases (58.33%, 7/12) had tree in bud pattern of distribution of nodules followed by miliary pattern (25%) and then centrilobular pattern in 16.6% of cases.

In addition, diagnosis of bacterial pneumonia in 5 (10%), PJP in 3 (6%), Viral pneumonia (CMV) in 2 (4%) and fungal infection 1 (2%) were reported. However, 15 (30%) subject did not show any abnormality. We observed that all cases of bacterial pneumonia showed patchy areas of air-space consolidation in all patients, centrilobular nodules in 60% (3/5) and non-necrotic mediastinal lymphadenopathy (40%, 2/5). We found that all PJP cases showed GGO with one patient crazy paving and one patient pneumatocele. CMV viral pneumonia displayed diffuse multi lobular ground glass opacities in bilateral lung with nodular shadowing. We observed one case of fungal infection presented with bilateral poorly defined few sub-centimetric nodules with surrounded by a halo of GGO (Table 2, Figure 2).

In current study, we found 4 (8%) cases of lung malignancy. Non-AIDS-defining cancers (NADCs) included 2 (4%) case metastasis from hepatocellular carcinoma (HCC), 1 (2%) case of primary adenocarcinoma of lung and AIDS-defining cancers (NADCs) included 1 (2%) case of metastasis from Non-Hodgkin's lymphoma (NHL) (Figure 3). One case (2%) of chronic kidney diseases (CKD) and one (2%) dilated cardiomyopathy (DCM) were found. We found 5 (10%) cases of pericardial effusion, out of which three patients of

Miliary TB, one patient with CKD and one patient had DCM with pericardial effusion (Table 2).

Final diagnosis versus CD 4 count

No significant correlation was found between CD4 count and pulmonary pathologies (Table 3).

Sensitivity, specificity, positive and negative predictive values of chest X ray

In our study, sensitivity of chest radiograph was 83%, specificity was 100%, positive and negative predictive values 100% and 71.43% respectively.

DISCUSSION

AIDS was first recognized in the United States in the 1981. In 1986, the first case of HIV was diagnosed in India. Progressive quantitative and qualitative deficiency of the subset of T- lymphocytes referred to as CD4 cells results in profound immunodeficiency in HIV patients.[5] Due to immunodeficiency, pulmonary infections are one of the most frequent causes of hospital admissions and death in HIV patients.[6] In consistent with numerous studies reported word wide, our study demonstrated the spectrum of OIs, malignancy, cardiomyopathy and CKD in HIV patients with low CD4 count.[2,7]

The CD4 cell count is an excellent indicator of immunity in HIV infected patients. Decrease in CD4 count below 500 cells/ μ l presages the development of clinical AIDS and a drop below 200/ μ l not only define AIDS but also indicates the high probability for the development of the AIDS related OIs and neoplasms.[2,5] In current study, the mean CD4 count was 232.5 ± 132 cells/ μ l which is comparable to a study conducted Ghate et al. and Antwal et al. [7,8] In addition, we didn't find significant correlation between CD4 count and pulmonary pathologies. This can be due to small sample size or not using a patient for comparison with CD4 counts more than 500 cells/ μ l. Similarly, Akinbami et al., didn't found correlation with CD4 count and pulmonary infections.[8]

In this study, mean age of HIV-positive patient was 37 years which is comparable to study done by Antwal et al., and Akinola et al., who reported that the majority of the cases occurred in the third and fourth decades of age.[7,10] In agreement with Antwal et al., we also found that more males were infected than females.[7]

One-third of patients with HIV are infected with PTB and diminished host immunity is a prejudicing cause and the utmost single risk factor.[11] In our study, we found 18 cases of PTB in HIV patients. Mean CD4 count of all type of TB cases were less than 300 cells/ μ l except old TB, and all patient with miliary TB had CD4 count less than 200 cells/ μ l. In the line of this, many studies are reported that there is increased risk of TB when CD4 count less than 300 cells/ μ l and further greater risk of miliary TB when CD4 count less than 200 cells/ μ l.[7,12] In our study, 83.3% (15/18) PTB patients had atypical patterns consisting of 16.6% (3/18) normal chest radiographs, 55.5% (10/18) patients showed infiltrates at the middle and/or lower zones, 33.3% (6/18) had mediastinal lymphadenopathy and 11.1% (2/18) presented with miliary TB. In accordance with San et al., we clinched that HIV patients with PTB who had CD4 count less than 300 cells/ μ l were more likely to present with atypical radiographic appearance.[13]

Among PTB patients, large number 66.7% were identified to have sub-centimetric nodular opacities on HRCT thorax. Similar to Kumar et al., in current study, majority (58.33%, 7/12) of cases with TB had nodular opacities with "tree-in-bud" pattern followed by miliary pattern (25%) and centrilobular pattern (16.6%).[14] Lymphadenopathy was noted in 44.4% (8/18) cases and majority of cases showed necrosis. This finding is similar to the study conducted by Feng et al., in which the presence of necrotic lymphadenopathy was a significant finding (77.2% cases) in HIV patients with PTB.[15] Mild cardiomegaly with pericardial effusion was noted in all cases of miliary TB, consistent with Barbarini and Barbaro.[16]

On CXR, lobar and multi-lobar consolidation are the major imaging finding observed in HIV positive patients with pyogenic infections.[5,17] We found 2 patients with normal chest radiograph, one patient with lobar consolidation, and two patients with infiltration with lymphadenopathy. In line with Nyamande et al., our study had shown that the high percentage (40%) of HIV patients with bacterial pneumonia have abnormalities that are not visible on chest

radiograph.[18] HRCT findings of bacterial pneumonia included patchy areas of air-space consolidations in all cases and centrilobular nodules in majority (60%) of patients. In agreement with this findings Atwal et al., reported that focal consolidation was the most common (approximately 67%) HRCT finding observed in bacterial infection.[19]

PJP remains the most common opportunistic pulmonary fungal infection in HIV with CD4 counts less than 200 cell/ μ l.[18,20] In our study, three HIV patients were diagnosed with PJP had mean CD4 count 97 cells/ μ l. All patients showed diffuse bilateral symmetrical interstitial infiltrate and ground glass opacities in perihilar distributions on radiographs. Likewise, HRCT thorax revealed GGO with perihilar distribution. One patient showed “crazy paving pattern” and one patient showed multiple variable sized cystic lesions with pneumothorax. Thus, our study confirmed that HRCT thorax is not only useful for detecting and characterizing PJP but also allowed increased diagnostic accuracy compared to chest radiograph.[20,21]

Cytomegalovirus (CMV) is responsible for more than 50% of immunosuppression-related viral pneumonia, particularly for those with T-cell defect.[11] In our study, there were two cases of CMV pneumonia with mean CD4 count 97 cell/ μ l, which was higher than previously mentioned studies.[20] On chest radiograph, we observed GGO, nodules, perihilar and lower zone interstitial infiltrates. In consistent with Franquet et al., CT thorax showed diffuse multi lobular ground glass opacities in bilateral lung with peripheral nodular shadowing. [22] On imaging it is difficult to differentiate CMV from PJP, however when ground-glass opacification is associated with nodularity and an effusion, CMV should be considered over PCP.

In our study, we observed one case of angioinvasive aspergillosis with CD4 count 106 cells/ μ l. He had cough and fever as symptoms with no findings on CXR. On CT thorax we detected bilateral poorly defined few (3-4) nodules, less than 1 cm in size with surrounded by a halo of GGO. Immunosuppressed patients, particularly neutropenic patients with CD4 count less than 200 cell/ μ l, are at high risk of developing invasive aspergillosis.[11,23]

Lee et al., found that 42% were ADCs and 58% were NADCs in HIV. The most common ADCs were NHL (53.6%), followed by Kaposi's sarcoma (17.9%). The most common NADCs were lung cancer (25%) and HCC (25%).[24] In consistent with this, we found 8% cases of lung malignancy, including 4% case metastasis from HCC, 2% case of adenocarcinoma of lung and 2% case of metastasis from NHL. In our study, the HIV patient with malignancies have mean CD4 count 230 cells/ μ l. Guiguet et al., found that the risk of lung cancer doubled when blood CD4 cell count < 500 cells/ μ l and the risk sustained to increase with further declines in CD4 counts.[25]

HIV affects multiple organs system, including the heart and kidneys. In the present study, only one (2%) patient had DCM with pericardial effusion. The basis of DCM is composite and multifactorial, including myocarditis secondary to HIV itself or other infectious agents, autonomic insufficiency, autoimmune factors, and cardiotoxicity of antiretroviral drugs.[16,26] In our study, we found only one case (2%) of CKD with CD4 count 160 cells/ μ l. Although multiple factor contributing into this, though high viral load and low CD4 count are predictive of HIV associated CKD.[27,28]

Other than above findings, we found 15 (30%) patients without any findings on CXR as well as on HRCT thorax. The mean CD4 count in this group was 260 ± 160 cells/ μ l. In addition, we observed that six patient (12%) who had “normal” radiograph were found to have abnormalities on HRCT thorax. Two of them diagnosed as primary TB, one reactivation TB, one angioinvasive aspergillosis and two bacterial pneumonia. In consonance with Kang et al., 1996 in current study HRCT was more sensitive and specific than chest radiography in detection of pulmonary infection and tumor in HIV and the sensitivity and specificity of chest radiograph was 83% and 100%, respectively.[29]

CONCLUSION

Radiography has shown good sensitivity and specificity, though it is inconclusive in significant number of HIV patients. HRCT characterized and categorized the lesions, thus helped to plan timely management and reducing the morbidity and mortality from respiratory pathologies in HIV patients. Hence, we endorsed HRCT

thorax in the diagnosis, management, and follow up of pulmonary diseases in HIV patients, as its non-invasive, easily available, cost-effective, highly sensitive and specific with faster scan time make it a suitable choice.

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Table 1: Distribution of Abnormal HRCT Findings

HRCT Findings	Number of Patients	Percentage (%)
Nodules	19	38.0
GGO	14	28.0
Lymphadenopathy	11	22.0
Fibro-Bronchiectasis	10	20.0
Pleural Effusion	8	16.0
Consolidation	7	14.0
Pericardial Effusion	5	10.0
Malignancy	4	8.0
Cardiomegaly	3	6.0
Emphysema	3	6.0
Cavitation	2	4.0
Empyema	1	2.0

Table 2: Final Diagnosis Versus Mean CD 4 Count

Final Diagnosis	Number of patients	Percentage (%)	Mean CD4	SD	Range (Min-Max)
Active TB (Primary)	7	14.0	235	151.8	64 - 452
Active with OLD TB (Reactivation)	5	10.0	270.4	67.6	202 - 370
Bacterial Pneumonia	5	10.0	262.6	140.9	42 - 367
Metastasis	3	6.0	204.7	96	108 - 300
Miliary TB	3	6.0	138.3	104	17 - 199
Old TB	3	6.0	310.3	135.8	154 - 399
P. jiroveci Pneumonia (PJP)	3	6.0	106.7	85.05	20 - 190
Viral Pneumonia (CMV)	2	4.0	97.50	41.8	68 - 127
Aspergillosis	1	2.0	106	-	-
CKD	1	2.0	160	-	-
Lung Malignancy	1	2.0	308	-	-
DCM with Pericardial Effusion	1	2.0	303	-	-
Normal	15	30.0	206.8	160.8	21 - 499
Total	50	100.0	232.5	132.1	17 - 499

Table 3: Final diagnosis versus CD 4 counts and p-value. In this study the level of significance was set at $p < 0.05$ and there was no significant correlation with CD4 count and pulmonary pathologies.

FINAL DIAGNOSIS	CD4 Count			Total	p-value
	≤ 200 (n=24)	201 – 400 (n=22)	> 400 (n=4)		
TB	8	9	1	18	0.733
Bacterial Pneumonia	2	3	0	5	0.656
Malignancy	1	3	0	4	0.411
Pneumocystis jiroveci Pneumonia (PJP)	3	0	0	3	0.177
Viral Pneumonia (CMV)	2	0	0	2	0.323
Angioinvasive Aspergillosis	1	0	0	1	0.575
DCM with Pericardial Effusion	0	1	0	1	0.575
CKD	1	0	0	1	0.575

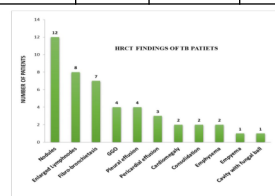


Figure 1: Distribution of Abnormal HRCT Findings in TB Patients

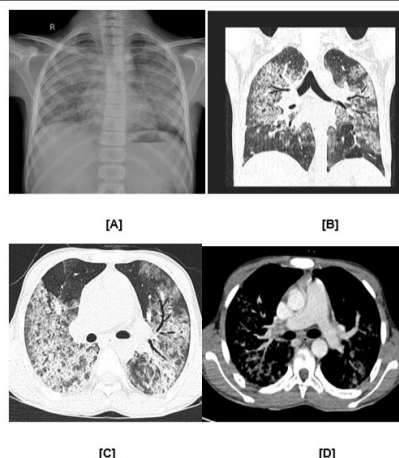


Figure 2: Pneumocystis jirovecii pneumonia (PJP) in 18-year-old HIV male with a CD4 count 20 cells/ul. The chest radiograph shows perihilar ground-glass appearance in the shape of bats-wings. Computed tomography (CT) in showing foci of consolidation and interlobular septal thickening due to organized inflammatory infiltrate and ground-glass attenuation with a geographic or mosaic distributions.

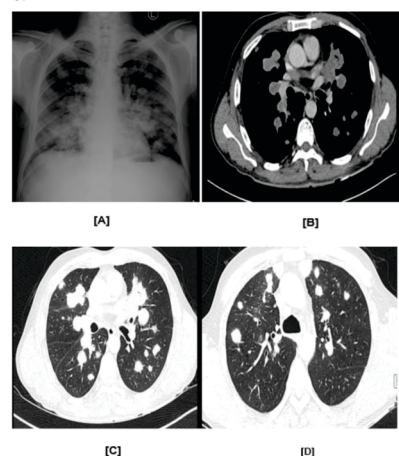


Figure 3: NHL with lung metastasis in a 43-year-old HIV male. The chest radiograph shows multiple well-defined lung nodules within the bilateral lung fields. No mediastinal Lymphadenopathy as it is a not a feature in AIDS-related NHL. These findings are confirmed by computed tomography showing multiple heterogeneously enhancing parenchymal and pleural based variable sized nodules.

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