

Original research article

Study is to Establish the Role of HRCT of Chest in the Early Diagnosis Of Pulmonary Disease in Symptomatic HIV Seropositive Patients With Normal Chest Radiograph.

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Abstract

World wide it is estimated that 40.3million patients are living with Human Immunodeficiency Virus (HIV) and 90% of these are in developing countries. About 70% of patients with HIV infection experience a pulmonary complication during life, and additional pulmonary pathology is often unexpected finding at autopsy. The clinical and radiographic presentation of lung disease associated with HIV infection is non-specific. Chest radiography has limited sensitivity for the detection of early infection in immunocompromised patients. The absence of radiographic findings however does not rule out pulmonary disease. Tuberculosis (TB) being the main opportunistic pulmonary infection contributing to mortality among HIV infected individuals, it is important to diagnose and treat it early. The present study is undertaken to establish the role of CT scan, particularly thin section CT (HRCT), in the early diagnosis of pulmonary disease in symptomatic HIV seroreactive patients with normal chest radiograph. 56 HIV seropositive patients who had pulmonary complaints with normal chest radiograph were selected. A HRCT scan of the chest was performed, HRCT findings were correlated with clinical features and other investigations. 19 (36.53%) out of 52 patients with normal chest radiograph had abnormal HRCT chest findings. HRCT of the chest should be done and must be included in the diagnostic algorithm for detecting early lesions in HIV seropositive patients with pulmonary symptoms with normal chest X- ray.

Key words: HIV patients, HRCT chest , Normal chest radiograph, Pulmonary disease.

Introduction

AIDS (Acquired Immune Deficiency Syndrome) was first recognized in the United States in the summer of 1981, when the U.S.(United States) Centers for Disease Control and Prevention (CDC) reported the unexplained occurrence of *Pneumocystis jiroveci* (formerly *P. carinii*) pneumonia (PCP) in five previously healthy homosexual men in Los Angeles and of Kaposi's sarcoma (KS) with or without *P. jiroveci* pneumonia in 26 previously healthy homosexual men in New York and Los Angeles⁽¹⁾. Since that time pulmonary infections have accounted for much of the morbidity and mortality related to this infection. World wide it is estimated that 40.3million patients are living with Human Immunodeficiency Virus (HIV) and 90% of these are in developing countries. About 70% of patients with HIV infection experience a pulmonary complication during life, and additional pulmonary pathology is often unexpected finding at autopsy. The burden of HIV related pulmonary disease in developing countries is therefore immense. ⁽²⁾ The three most important and common

pulmonary complications of HIV are tuberculosis, PCP and bacterial pneumonia. These comprise greater than 90% of pulmonary complications worldwide. In developing countries, bacterial infections (especially tuberculosis) are of much greater importance, perhaps because these virulent infections occur at an earlier state in the disease before the profound immune-suppression which is required for PCP.⁽³⁾ The clinical and radiographic presentation of lung disease associated with HIV infection is non-specific. Chest radiography has limited sensitivity for the detection of early infection in immunocompromised patients. The absence of radiographic findings however does not rule out pulmonary disease.^(4,5) In up to 10% of cases of both tuberculosis and PCP, the chest radiograph may be clear. Computerized Tomography (CT) scanning of chest, especially High Resolution Computerized Tomography (HRCT) may be useful by revealing lesions not apparent on chest radiography.⁽⁶⁾ HIV poses special problems in the diagnosis of tuberculosis. With the spread of HIV into every corner of Indian subcontinent, Tuberculosis (TB) being the main opportunistic pulmonary infection contributing to mortality among HIV infected individuals, it is important to diagnose and treat it early. More often it presents in atypical forms with rapid progression. Though pulmonary tuberculosis is the common form, extra pulmonary forms are increasingly seen in HIV and are particularly difficult to diagnose.⁽⁷⁾ In addition to these, sputum smear negativity for Acid Fast Bacilli (AFB) is more common in patients of HIV with tuberculosis. CT scanning may be useful in identifying pattern that suggests specific pulmonary pathology in tuberculosis, PCP etc.⁽⁸⁾ In some studies HRCT was shown more sensitive and more specific than Gallium scintigraphy in diagnosing pulmonary diseases early. HRCT has high positive and negative predictive values than gallium. HRCT is more helpful in guiding the method of biopsy and directing the bronchoscopist to the diseased lung segment that would maximize diagnostic yield.^(9,10)

The present study is undertaken to establish the role of CT scan, particularly thin section CT (HRCT), in the early diagnosis of pulmonary disease in symptomatic HIV seroreactive patients with normal chest radiograph.

Material and Methods:

The present observational study was done at Department of Pulmonary Medicine, Rajiv Gandhi Institute of Medical Sciences Adilabad, Telangana. Patients for the study were identified and studied at outpatient block. The study group included patients presented to the outpatient block at Rajiv Gandhi Institute of Medical Sciences Adilabad, Telangana, with respiratory complaints who were diagnosed and registered as HIV seropositive at any Integrated Counseling and Testing Centers (ICTC) for HIV, organized by Telangana State Aids Control Society, Hyderabad. Patients were subjected for CT scan evaluation of chest only after taking proper consent. Patients were explained properly and informed prior about the merits and demerits of CT scan imaging. Permission and clearance was given by the thesis ethics committee.

Cases with HIV infection and pulmonary complaints attending the Pulmonary medicine OP/Ward were included in study. According to the studies conducted by John Segreti *et al*⁽⁶⁾, the chest radiographs were normal in 10% of his HIV positive patients with pulmonary symptoms. So, in the present study, out of 482 HIV seropositive symptomatic patients, the sample size is expected to be 50. As per the previous similar study done by J. Raghu *et al*, the prevalence of positive findings in CT scan of HIV seropositive individuals with normal chest x ray was 38.7%. With the previous prevalence the sample size can be calculated. Accordingly, 56 patients who had pulmonary complaints with normal chest radiograph were selected. Out of the 56 patients who were investigated, 4 patients did not turn up for follow up with the investigation report. Only 52 are included in the present study.

Inclusion Criteria:

- HIV seropositive patients diagnosed at ICTC centers where 3 different types of rapid tests (Bioline method, Triline method, Trispot method) were performed to detect antibodies against HIV.
- HIV seropositive patients with symptoms suggestive of lung disease – fever, cough, breathlessness, chest pain, night sweats, generalized weakness, loss of appetite and weight etc.,
- Symptomatic HIV seropositive patients with Normal chest radiograph as confirmed by the thesis guide and radiologist.

Exclusion Criteria:

- HIV seronegative patients
- Asymptomatic HIV seropositive patients
- Patient with abnormal chest radiographs
- Patients less than 12 years of age
- Patients with other systemic diseases like heart disease, CNS problems, diabetes mellitus etc.,
- Pregnant woman
- Un co-operative patients

All cases were examined in detail as per proforma with special reference to respiratory system. Other systems were also examined in detail whenever it was found necessary. In each case, history of present and past illness was carefully enquired into so as to obtain a complete historical background of case. None of the patients were on antiretroviral therapy. After clinical examination all the patients were subjected to the following investigations:

Chest X-Ray PA View, Complete blood picture, urine – Albumin, Sugar and deposits, Blood sugar, Blood urea, Serum creatinine, Serum bilirubin, SGPT, Serum electrolytes, Absolute lymphocyte count, CD4+ count, SPO2 (oxygen saturation) measurement, Mantoux skin test, Sputum examination-Gram stain, culture, AFB smear examination (2 Sputum samples), oxygen saturation measurement, **HRCT**.

A HRCT scan of the chest was performed consisting of 1.5mm collimation section at 10mm intervals reconstructed with a high spatial frequency algorithm. All scans were performed without intravenous contrast media at suspended end inspiration with the patient in a supine position. Scans were reviewed at a setting appropriate for both lung parenchyma and mediastinum. The chest radiograph and HRCT scans were evaluated by a radiologist who had no prior knowledge of the etiology and clinical features. The HRCT scans were reported without the concurrent availability of the chest radiograph. HRCT findings were correlated with clinical features and other investigations.

Results

Out of 482 HIV positive cases treated and investigated at outpatient department, 56 (11.08%) patients had normal chest radiograph with pulmonary symptoms. But 4 patients were lost for follow up. So results were tabulated for 52 patients. This accounts for 10.78% of the total number of the cases. Out of the total 52 cases studied, most of the cases (48.07%) belong to the age group between 31-40 years; 36.53% of patients were in the age group of 21-30 years; 11.53% patients were in the 41-50 years age group and only 2(3.88%) patients had age less than 20 years. In the present study the patient's age ranged from 12 years to 50 years. Mean age of the group is 32.3 years. The maximum number of cases were between 31-40 years. Of the total number of 52 cases studied, 30(57.69%) were males and 22 (42.31%) were females.

The male: Female ratio is 1.3:1. This indicates that about 60% of the total cases were males and the female constituted 40% of the total.

Table 1: Clinical Presentations

Symptoms	No. of cases	Percentage(n=52)
Cough	50	96.15%
Dyspnoea	19	36.5%
Fever	38	73.07%
Chest pain	7	13.40%
Hemoptysis	6	11.52%
Others (night sweats, loss of appetite& weight, diarrhea, vomiting)	10	19.2%

In this study, 50 patients presented with cough (96.15%) as the main symptom. Fever was the main presenting symptom in 38 (73.07%) patients. Dyspnoea was seen in 19 (36.5%) of cases while chest pain was seen in only 7 (13.40%) of cases. Hemoptysis was seen in 6 patients(11.52%). Other symptoms like night sweats, loss of appetite, loss of weight, wheeze, diarrhea, vomiting were seen in 10 (19.2%) of the cases. The most common symptoms observed in the present study were cough (96.15%) and fever (73.07%).

Table 2: Patients with normal & abnormal HRCT.

HRCT finding	No. of cases	Percentage(n=52)
Abnormal CT	19	36.53%
Normal CT	33	63.47%

The present study shows that about 36.53% of the patients with normal chest radiograph and pulmonary symptoms had abnormal HRCT findings. While, 63.47% of the patients had normal HRCT findings. Mantoux skin test was positive in 16 patients (30.76%) out of the 52 cases studied. Of these, 9 patients were males and 7 patients were females. The Mantoux skin test was negative in 36(69.24%) of the cases studied.

Table 3: Percentage distribution of positive HRCT chest findings

HRCT findings	No. of patients	Percentage (n=52)	Male%	Female%
Blebs	1	1.92%	1(1.92%)	0(0%)
Areas of pneumonitis	3	5.76%	2(3.84%)	1(1.92%)
Consolidation	3	5.768%	1(1.92%)	2(3.84%)
Infiltrations	12	23.04%	4(7.68%)	5(9.61%)
Ground glass opacity	5	9.61%	4(7.68%)	1(1.92%)
Broncho pneumonia	1	1.92%	0(0%)	1(1.92%)
Pleural effusion	1	1.92%	1(1.92%)	0(0%)
Hilar adenopathy	3	5.76%	1(1.92%)	2(3.84%)
Cavities	3	5.76%	1(1.92%)	2(3.84%)

Of all the CT findings observed, Infiltrations were seen in 12 cases (23.04%), ground glass opacities in 5 cases (9.60%), areas of consolidation seen in 3 cases (5.76%), hilar adenopathy, areas of consolidation, areas of pneumonitis and cavities in 3 cases (5.76%) each, blebs, pleural effusion and bronchopneumonia in 1 case (1.92%) each with 4 male (7.68%) and 5 female (9.61%). Hilar lymphadenopathy, areas of consolidation and Cavities were seen in 3 cases each (5.76%), 1 male (1.92%) and 2 females (3.84%) in both CT findings. Pleural Effusion, Blebs and Broncho pneumonic pattern were seen in 1 patient each (1.92%). Pleural Effusion and Blebs were seen in 1 male each and Bronchopneumonia pattern seen in 1 female.

Table 4: Comparison of mantoux skin test result with HRCT findings

Mantoux test	Abnormal CT	Normal CT	Total
Positive	9(17.3%)	7(13.4%)	16(30.76%)
Negative	10(19.2%)	26(50%)	36(69.24%)
TOTAL	19(36.53%)	33(63.46%)	52(100%)

This table compares the number of abnormal and normal HRCT findings in Mantoux positive and negative individuals. 9 (17.3%) out of 16 patients with Mantoux positivity showed abnormal HRCT. While 10(19.2%) out of 36 patients with Mantoux negativity showed abnormal HRCT findings. This table interprets the importance of Mantoux skin testing in symptomatic HIV seropositive individuals presented with normal Chest X-ray, and were investigated further with HRCT.

Table 5: Statistics of diagnosis made in this study

Diagnosis	No. of cases	Percentage of total (%) (n=52)
Pulmonary Tuberculosis	10	19.2%
Extrapulmonary tuberculosis	1	1.92%
Bacterial Pneumonia	2	3.84%
Pneumocystis carinii pneumonia	3	5.76%
Others (pneumonitis, OAD)	3	5.76%

In our study the most common diagnosis was tuberculosis with 11 cases (21.15%) of total. Bacterial pneumonia accounted for 2 cases (3.84%). PCP was seen in 3 cases (5.76%). Others included Blebs OAD (Obstructive Airway Disease) seen in 1 case (1.92%) and nonspecific Lower Respiratory Tract infection in 3 cases (5.76%). So in the present study most common diagnosis with normal chest X-ray was Tuberculosis.

Discussion

In our study of 482 HIV seropositive patients with pulmonary symptoms, 56 patients were selected for study that had normal chest radiograph which is equivalent to 11.08%. This value correlates with the studies conducted by John Segreti *et al*, who demonstrated that the chest radiographs were normal in 10% of his HIV positive patients with pulmonary symptoms.⁽⁶⁾ Among these 56 patients, 4 patients did not turn up for further investigations. Hence only 52 patients were included in the study. The most common presenting symptoms in our study were cough (96.15%), fever (73.07%) and dyspnoea (36.5%). In 1 patient dyspnoea was the major complaint. All the 52 patients were examined clinically, followed by laboratory examinations and high resolution- CT of the chest was done within a week. Out of these 52 patients with normal chest radiographs, 19 patients had abnormal HRCT findings,

which is equivalent to 36.53%. In a study conducted by Kauczor H U, Schnutgen M *et al* in 1995, HRCT was done on 30 HIV seropositive patients with respiratory complaints and normal chest radiographs, of which 30.77% had abnormal findings.⁽¹¹⁾ In another study conducted by Diehl SJ, Lehmann KJ *et al* in 1997, 31 HIV seropositive cases with acute pulmonary symptoms and normal or non specific chest radiographs, HRCT was done. Nineteen of these patients (61.3%) showed abnormal HRCT findings. This high value could be due to the inclusion of cases with non-specific chest radiographs.⁽¹²⁾

These two studies concluded that in the presence of pulmonary symptoms in HIV seropositive patients, HRCT should be performed whether the chest radiograph is normal or abnormal since it may reveal additional information. Compared to Broncho Alveolar Lavage (BAL) and induced sputum, HRCT can provide conclusive results within a short time. This conclusion holds good even in the present study. In the present study, 84.61% of patients belonged to the age group ranging from 20 to 40 years with a mean age of 30.3 years. As this is economically the most productive age group, early diagnosis and treatment of pulmonary disease decreased the morbidity, mortality and economic burden on the society. Palmieri F, Girandi E *et al*, in their retrospective study on 146 HIV seropositive patients observed a decrease in survival among patients with pulmonary TB with negative sputum smear and normal chest X-ray at presentation. This was primarily attributed to the delay in the diagnosis of tuberculosis and initiation of anti-tuberculous treatment which resulted in rapid progression of HIV infection.⁽¹³⁾ This highlights the importance of early diagnosis and treatment in symptomatic HIV seropositive patients with normal chest x-ray findings in India, where tuberculosis contributes the major share for the morbidity and mortality of HIV infection. In the present study, the following were the CT findings – Infiltrations in 12 cases (23.04%), ground glass opacities in 5 cases (9.60%), areas of consolidation seen in 4 cases (7.68%), hilar adenopathy and cavities in 3 cases (5.76%) each, blebs, pleural effusion and bronchopneumonia in 1 case (1.92%) each. These findings can help us to suspect a diagnosis and guide us in selecting necessary, specific, invasive and laborious investigations like bronchoscopy, BAL, FNAC, sputum culture for TB bacilli, staining for *Pneumocystis carinii* etc., to come to a specific diagnosis. In the present study, 11 (21.15%) patients were diagnosed tuberculosis based on HRCT findings and other investigations like sputum examination for AFB, Mantoux test along with their clinical features. Patients were started on antituberculous treatment. Symptoms subsided in all cases within two to three weeks. Raninga S, Parikh N, Arora A *et al* recommended HRCT where X-ray findings are normal or inconclusive of tuberculosis in clinically suspected patients for confirmation and determination of activity. In the present study tuberculosis could be diagnosed based on HRCT findings, clinical features and other relevant investigations.⁽¹⁴⁾ In the present study 5 cases showed ground glass appearance in HRCT, dyspnoea being the main complaint in these patients. They were tachypnoeic with low oxygen saturation (low SpO₂). These patients were started on cotrimoxazole based on HRCT findings. They responded to treatment within 1 week. Gruden JF, Huang L *et al* confirmed that HRCT was 100% sensitive and 89% specific with 90% accuracy in diagnosing PCP.⁽¹⁵⁾ In 2 cases (3.84%) bacterial pneumonia was diagnosed based on clinical features, HRCT and sputum culture and treated with appropriate antibiotics. They responded to treatment within a week.

The relationship between smokers and their abnormal HRCT findings in the present study was not significant. Similar results were seen in the study by Raghu *et al* where there was an insignificant relationship between smokers and their abnormal HRCT findings.⁽¹⁶⁾ In 33 patients with normal chest X-ray and normal HRCT, the respiratory complaints might be due

to upper respiratory infections or other nonspecific airway diseases. They were treated symptomatically and they responded to the treatment.

Conclusion

Despite the development of effective therapies and better prophylaxis of opportunistic infections, pulmonary complications of HIV/AIDS remain an important cause of morbidity and mortality. Though chest X-ray remains the mainstay of thoracic imaging in HIV-infected patients, the absence of changes in chest radiograph should not exclude the diagnosis of pulmonary disease. CT/HRCT of chest plays an important role in establishing an accurate diagnosis when CXR findings are equivocal or non-specific. HRCT of chest is a useful cost-effective investigation that can help in suspecting a probable diagnosis of pulmonary diseases and start empirical treatment early before reaching a definitive diagnosis using invasive and laborious investigations. Furthermore, HRCT of chest is superior in demonstrating the distribution and extent of parenchymal abnormalities and can localize the lesions in the lungs and helps further diagnostic accuracy in invasive investigations. So, it may be concluded that HRCT of the chest should be done and must be included in the diagnostic algorithm for detecting early lesions in HIV seropositive patients with pulmonary symptoms with normal chest X-ray, before contemplating for invasive investigations like bronchoscopy, BAL & FNAC etc., as it may reveal additional information and may help to avoid unnecessary delay and allows early medical intervention in treating the pulmonary disease.

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