

# Pulmonary Manifestations in HIV Seropositive Patients and Their Correlation with CD4 Counts in a Tertiary Care Centre of North India

Ravinder Pal Singh, Anil Kumar Kashyap, Sandeep Puri, Jagdeep Whig\*

## Abstract

The prolonged course of human immunodeficiency virus (HIV) infection is marked by a decrease in the number of circulating CD4+ T helper cells and persistent viral replication, resulting in immunologic decline and death from opportunistic infections. The study was conducted in HIV Seropositive Patients admitted in our hospital. Demographic profile of the patient was recorded along with history, examination, investigations and evaluated for pulmonary manifestations and correlated with the CD4 counts. Age of HIV positive cases ranged from 21 to 74 years, male: female ratio was 3:1. Commonest mode of transmission was heterosexual sex (77%) followed by IV drug abusers (13.3%). Commonest X-ray finding was Infiltrates (33.3%) followed by pleural effusion (8%) and miliary mottling (5.3%). Commonest pulmonary diagnosis was pulmonary tuberculosis in 22.6% cases, followed by pyogenic pneumonia in 14.67% and pneumocystis carinii pneumonia (PCP) in 5.3% cases. Extrapulmonary tuberculosis was present in 16% of the cases. Pulmonary tuberculosis and pyogenic pneumonia was present in over wide range of CD4 count but their incidence has increased as the CD4 count declined. The knowledge of the CD4 count level in HIV patients is extremely useful in making differential diagnosis and suggesting a diagnostic and therapeutic plan.

## Key Words

HIV, Pulmonary manifestations, CD4 Counts

## Introduction

AIDS the acquired immunodeficiency syndrome is a fatal illness caused by retrovirus known as human immunodeficiency virus which breaks down body's immune system leaving the victim vulnerable to host of life threatening opportunistic infections, neurological disorders and malignancies (1).

The prolonged course of human immunodeficiency virus (HIV) infection is marked by a decrease in the number of circulating CD4+ T helper cells and persistent viral replication, resulting in immunologic decline and death from opportunistic infections and neoplasms (2).

Associated symptoms with this initial stage of infection occur to varying degrees of severity and may

include fever, sore throat, skin rash, lymphadenopathy, splenomegaly, myalgia, arthritis and less often meningitis (3). The acute phase is followed by a clinically latent period with low level viral replication and a gradual fall in CD4 count where the patient can remain asymptomatic for several months to years. In India, the mean duration of survival after diagnosis of HIV is 92 months. Patients with CD4 counts less than 200 cells/ $\mu$ l are 19 times more likely to die than those with CD4 counts greater than 350 cells/ $\mu$ l (4).

Pulmonary complications have been one of the commonest causes of morbidity and mortality since the advent of AIDS (5). Pulmonary symptoms may result

From the Deptt. of Medicine, Dayanand Medical College & Hospital & Apollo Hospital,\* Ludhiana Ludhiana, 141001, Pb - India  
Correspondence to : Dr. Anil Kumar Kashyap, Assistant Professor, Department of Pulmonary Medicines, Dayanand Medical College & Hospital, Tagore Nagar, Civil Lines, Ludhiana, 141001, Punjab, India

from a wide spectrum of pulmonary illness that include both opportunistic infections which include bacterial, mycobacterial, fungal, viral, parasitic pathogens and neoplasms. This study is therefore aimed at evaluating the pattern of respiratory complications amongst HIV seropositive patients.

### Material and Methods

The present study was conducted in patients who were HIV Seropositive admitted in medical wards of Dayanand Medical College & Hospital, Ludhiana in 17 months duration. The diagnosis of HIV infection was made by HIV enzyme-linked immunosorbent assay (ELISA) method and confirmed by western blot method in low risk individuals. After confirmation of the positive HIV status, informed written consent was taken and patients were enrolled consequently.

A detailed clinical history was taken and recorded, data on demographic profile of individuals age, sex, residence and marital status was collected. Risk factors for HIV infection and mode of transmission was noted. All the presenting complaints with mode of duration of each were noted with more emphasis on respiratory symptoms. Various investigations which were conducted were complete blood count (CBC), erythrocyte sedimentation rate (ESR), CD4 count, chest X-ray, sputum examination including sputum for acid fast bacilli (AFB) smear two times, AFB culture in those who have already taken antitubercular therapy, sputum for culture sensitivity, gram stain, fungal smear, sputum for pneumocystis jiroveci cyst was sent. Computed tomography (CT) chest was done wherever required.

**Table 1. CD4 Lymphocytes Counts in Relation to Number of Presenting Complaints**

No of presenting complaints	No. (%)	Mean CD4 count $\pm$ SD (cells/ml)	Correlation Coefficient
0-2	19 (27.14%)	250.79 $\pm$ 218.64	<b>r = - 0.252</b> <b>P &lt; 0.05</b>
3-4	26 (37.14%)	120.42 $\pm$ 82.01	
5-6	20 (28.57%)	132.55 $\pm$ 147.09	
7-8	5 (7.14%)	82.6 $\pm$ 98.24	
Total	70	156.57 $\pm$ 158.08	

*SD= Standard Deviation; p-value = Probability Value; r = Coefficient of correlation*

The diagnosis of pulmonary manifestations was made on the basis of detailed clinical history, general physical and systemic examination, radiographic findings, and sputum analysis. Pleural fluid was tapped where applicable and was sent for biochemistry, cytological and microbiological analysis including culture sensitivity, adenosine deaminase (ADA), gram staining and Acid fast bacilli.

Pulmonary manifestations of all the patients were noted and correlated with their CD4 counts. CD4 count was divided into four groups. Group 1 included patients with CD4 counts less than 100/ $\mu$ l, group 2 included those having CD4 counts between 100-199/ $\mu$ l, Group 3 included patients with CD4 counts between 200-399/ $\mu$ l while group 4 included those having CD4 < 400/ $\mu$ l.

### Statistical Analysis

The collected data was analysed by means, standard deviations, percentages and correlation analysis by using Microsoft excel. MS Office's excel and word was used to generate the tables.

### Results

In the 17 months Period of the study 75 cases of diagnosed HIV infection who were admitted in Dayanand Medical College and Hospital Ludhiana were enrolled. Of the 75 cases enrolled 56 (75%) were males and 19 (25%) were females with a male to female ratio of 3:1. The age of cases ranged from 21-74 years with a mean age of 40.45 yrs (SD  $\pm$  12.01). Among the 75 cases, 64 (85%) were married and 11 (15%) were unmarried. Heterosexual sex was the most common route of transmission in 58 (77%) of the cases, while 7 (9.33%) cases were found to have history of blood transfusion and 10 (13.33%) cases were intravenous drug abusers. Fever was the most common symptom (70%) followed

**Table 2. X-ray Findings in HIV Positive Cases**

Finding	No. of cases (n=75)	% age
Infiltrates	25	33.3
Pleural effusion	6	8
Cardiomegaly	2	2.66
Calcification	2	2.66
Fluid overload	2	2.66
Reticulonodular shadow	1	1.33
Pneumothorax	2	2.66
Military mottling	4	5.33
Pulmonary fibrosis	1	1.33
Normal	36	48

**Table 3. Distribution of Cases According to Pulmonary Diagnosis and Relation to CD4 Counts**

Pulmonary diagnosis	No (n= 35) (%)	No. of cases with CD4/ $\mu$ l			
		0-99	100-199	200-399	=400
Tuberculosis	17(48.6)	9	4	3	1
Pyogenic pneumonia	10(28.6)	3	3	3	1
Fungal pneumonia	1(2.85)	0	1	0	0
PCP	4(11.4)	3	1	0	0
Nocardia	1(2.85)	1	0	0	0
Pneumothorax	1(2.85)	1	0	0	0
Fungal and Pyogenic pneumonia	1(2.85)	1	0	0	0

*n = number of patients; percentage is in parentheses*

by anorexia (56%), breathlessness (52%) and weight loss (49.33%). Cough was present in 42.66% cases, expectoration in 33.33% cases and neurological symptoms in 24% cases. Diarrhoea was seen in 18.66% and chest pain in only 9.33% of patients.

Lymphadenopathy was present in only five cases (6.66%), supraclavicular lymph nodes in three cases, one case each of inguinal lymph nodes and cervical lymph nodes. Seventy (93.3%) patients were found to be anaemic (Hb < 13g/dl), severe anaemia (Hb < 7g/dl) was found in eleven (14.7%) cases. Mean TLC was found to be  $10.78 \times 10^3/\mu$ l. ESR done in sixty nine cases, raised in all cases except one.

**CD4 Counts:** The CD4 count was done in seventy patients while CD4 count in five cases was not known. . The CD4 count mean was 157/ $\mu$ l and median 112/ $\mu$ l. Over 47% of cases (33/70) had CD4 count less than 100/ $\mu$ l, and about 70% of the cases had CD4 count less than 200/ $\mu$ l. CD4 count in relation to number of presenting

complaints are shown in *Table 1*. Thus it was interpreted that if the number of the presenting complaints of HIV positive patients was more, then the corresponding CD4 counts were less.

**Radio imaging:** Chest X-ray was done in all cases and it showed abnormality in 39 (52%) cases. X-rays findings in HIV positive cases are shown in *Table 2*. Infiltrates were present in 47% cases of 17 diagnosed pulmonary tuberculosis patients. CT Chest was done only in three cases, pulmonary tuberculosis (TB) with endobronchial spread was seen in one case, the second case showed multiple mediastinal lymph node necrosis with peripheral ring enhancement suggestive of tuberculosis while third case showed feature of extensive ground glass haze with septal thickening and multiple lung cyst suggestive of pneumocystis carinii pneumonia (PCP).

**Microbiology:** Sputum analysis was done in 29 cases out of 75. AFB was positive in only four cases while gram stain was positive in seven cases. Two patients

showed presence of gram positive cocci and the two had gram negative bacilli. Three patients showed the presence of both gram positive cocci and gram negative bacilli. Sputum culture confirmed acinetobacter and E.coli in one case each of pyogenic pneumonitis. One of the cases showed nocardia and candida was grown in two cases.

Pleural fluid analysis was done in seven (9.3%) cases, six cases of pleural effusion and one case of pyopneumothorax. On the basis of biochemistry, cytology, culture, staining and ADA reports, it was found to be tubercular in six cases and pyogenic in one case. Pleural AFB was positive in one case of pleural effusion.

**Pulmonary Diagnosis:** In our study, the pulmonary manifestations were seen in 35 (46.7%) cases with tuberculosis 17 (22.6%) as commonest manifestation (Table 3). Tuberculosis included all the cases of recently diagnosed pulmonary TB (7 cases), miliary TB (4 cases) and tubercular pleural effusion (6 cases). Similarly the pyogenic pneumonia included 8 cases of pyogenic pneumonitis, one case of pyopneumothorax and aspiration pneumonitis each. One case was seen to be having both pyogenic and fungal pneumonia. Relation of pulmonary manifestations with CD4 counts indicates that the incidence of all these manifestations increased with the decline of CD4 counts (Table 3).

**Non pulmonary opportunistic infections:** Extra pulmonary tuberculosis was present in twelve cases. Out of these, one case each of tubercular meningitis and bony tuberculosis, two cases having disseminated TB, four cases each of abdominal TB and tubercular lymphadenopathy were seen. Oral candidiasis was found in eight cases while cryptococcal meningitis in four cases and diarrhoea was found in eight cases.

## Discussion

In this study male predominance over females were similar to the incidence reported in other part of India. Majority of the cases were between 21 to 40 yrs of age. Similar demographic profile with young male predominance has been observed by other studies (6, 7). Studies from developing countries report heterosexual route as the most common mode of spread. In a study (6) of 377 HIV positive cases in Brazil, the most common mode of spread was heterosexual contact (65.8%) and similarly it was 60% in one study from India (7). In our

study sexual transmission mainly by heterosexual route was the predominant mode of transmission in both males and females.

Vanhems and colleagues observed fever, fatigue and myalgia as being the most common clinical manifestations (8). In our study, fever is the most common clinical manifestation found in 70% cases, other manifestation found are anorexia, breathlessness, weight loss, cough, neurological complaints and diarrhoea.

In a study conducted by Chakravarty *et al* (9) in 438 HIV positive patients, CD4 counts were significantly inversely correlated with the number of symptoms and the number of opportunistic infections (correlation coefficient were -.289 and -.236 respectively and  $p < 0.001$ ). Similarly in our study, significant inverse correlation was noted between CD4 count and number of symptoms ( $r = -0.252$  and  $P < 0.05$ ). Anemia characteristic of advanced illness was detected in majority of the cases in our study, strengthening the hypothesis of delayed diagnosis.

Study conducted by Swaminathan (10) showed that HIV seropositive patients with pulmonary TB were having normal chest radiographs in 14.2% cases, miliary TB in 10% cases, pleural effusion in 16.6%, cavitations in 17.8%, while maximum number of cases (65%) showed infiltrates. Similarly the study conducted by Perlman DC *et al* also showed infiltrates in maximum (43.75%) of cases of HIV positive pulmonary tuberculosis (11). In our study, 17 cases of pulmonary tuberculosis were diagnosed and X-ray findings in these cases showed infiltrates in 47% of cases which was almost similar to the previous studies. Pulmonary manifestations of HIV disease differ globally due to differences in current availability of effective HAART programs. In resource-limited settings, AIDS-related infectious complications such as Pneumocystis carinii pneumonia and pulmonary tuberculosis still predominate (12). In our study, pulmonary manifestations were present in 46.7% of cases.

In a study conducted in western Maharashtra (13), India, tuberculosis was the most common opportunistic infection with an incidence of 17%. In a study from United States, of 1246 HIV infected cases, mycobacterium tuberculosis was the least common opportunistic infection with an incidence of 1-2 events per 100 person year (14).

Kaposi sarcoma, atypical mycobacterial infection and disseminated Cytomegalovirus disease, which are common in western literature, was not seen in India (15). Similar trends were observed in other studies from other parts of India (16). In our study, mycobacterium tuberculosis was the most common pulmonary manifestation. Other pulmonary manifestations found were PCP, nocardia, pyogenic, fungal pneumonia. In previous studies, the prevalence of pleural effusion in hospitalized patients with AIDS varies from 7 to 27 percent (17) comparable with our study.

In India, the most common opportunistic infection among people with HIV infection is pulmonary tuberculosis (4). TB is unique in that it can occur over a wide range of CD4 count, although it is more frequent at CD4 counts < 300/ $\mu$ l (18). Studies have shown that there is a higher prevalence of diseases such as bacterial pneumonia and tuberculosis as the CD4 count level declines (5). This is concomitant with findings in our study in which incidence of tuberculosis and bacterial pneumonia has increased as CD4 count declined.

PCP almost always occur when CD4 count is < 200 / $\mu$ l and this is the level at which prophylactic therapy is given. The pulmonary complications of HIV infection study found that within 6 months of the CD4 count dropping below 300/ $\mu$ l, 15 % of patients not receiving prophylactic treatment developed PCP (19). Studies from Delhi and Chennai reported median CD4 count of patients with PCP of 142 and 87 cells / $\mu$ l respectively (18). Similarly in our study, all the 4 cases of PCP have CD4 count below 200 cells / $\mu$ l and out of them majority of cases have CD4 count below 100/ $\mu$ l.

### Conclusion

The most common pulmonary manifestation in HIV patients was pulmonary tuberculosis followed by pyogenic pneumonia, pneumocystis carinii pneumonia and fungal pneumonia and incidence of all these manifestations increased with the decline of CD4 counts. Knowledge of the pattern of pulmonary complications in patients with HIV infection in relation to CD4 count will help clinicians develop faster diagnostic and therapeutic approach to patient management.

### References

1. Park K. Epidemiology of communicable diseases AIDS. In: Text book of preventive and social medicine 22nd ed. Jabalpur: M/s Banarsi Dass Bhanot Publishers; 2013. pp. 316.
2. Pantaleo G, Fauci AS. Immunopathogenesis of HIV infection. *Annu Rev Microbiol* 1996;50:825-54.
3. Fauci AS, Pantaleo G, Stanley S, Weissman D. Immunopathogenic mechanisms of HIV infection. *Ann Int Med* 1996;93:4386-91.
4. Kumarasamy N, Solomon S, Flanigan TP, et al. Natural history of human immunodeficiency virus disease in southern India. *Clin Inf Dis* 2003;36:79-85.
5. Peters EJ, Essien OE. CD4 count levels and pattern of respiratory complications in HIV seropositive patients in Calabar, Nigeria. *Nigerian J Physiol Sci* 2007;22:93-7.
6. Sampio M, Sampio J, Haguilara, T, Ventin OF, Brites C. Clinical and laboratory Profile of HIV-positive patients at the moment of diagnosis in Bahia, Brazil. *Brazilian J Infectious Diseases* 2007;11:395-8.
7. Kothari K, Goyal S. Clinical presentation, spectrum of systemic involvement and opportunistic infections in AIDS patients. *J Assoc Physicians India* 2001;49:435-8.
8. Vanhems P, Routy JP, Hirschel B, et al. Clinical features of acute retroviral syndrome differ by route of infection but not by gender and age. *J AIDS* 2002;31:318-21.
9. Chakravarty J, Mehta H, Parekh A, et al. Study on clinic-epidemiological profile of HIV patients in Eastern India. *J Assoc Physicians India* 2006;54:854-7.
10. Swaminathan S, Narendran G, Menon PA, et al. Impact of HIV infection on radiographic features in patients with pulmonary tuberculosis. *Indian J Chest Dis Allied Sci* 2007;49:133-6.
11. Perlman DC, el-Sadr WM, Nelson ET, et al. Variation of chest radiographic patterns in pulmonary tuberculosis by degree of human immunodeficiency virus-related immunosuppression. *Clin Inf Dis* 1997;25:242-6.
12. Hull MW, Philips P, Montaner JS. Changing global epidemiology of pulmonary manifestations of HIV/AIDS. *Chest* 2008;134:1287-98.
13. Giri PA, Deshpande JD, Phalke DB. Prevalence of pulmonary tuberculosis among HIV positive patients attending antiretroviral therapy clinic. *North Am J Med Sci* 2013;5:367-70.
14. Moore RD, Chassin RE. Natural history of opportunistic disease in an HIV infected urban clinical cohort. *Ann Intern Med* 1996;124:633-42.
15. Mehta AA, Kumar VA, Vithalani KG, Patel KR. Clinico-epidemiological profile of HIV in Patients with respiratory infections and Tuberculosis in Western India. *J of Clinic & Diag Res* 2011;5:206-9.
16. Swaminathan S, Subbaraman R, Venkatesan P, et al. Tuberculin skin test results in HIV infected patients in India: Implications for latent tuberculosis treatment. *Int J Tuberc Lung Dis* 2008;12:168-73.
17. Afesa B. Pleural effusion and pneumothorax in hospitalized patients with HIV infection: the pulmonary complications, ICU support, and prognostic factors of hospitalized patients with HIV (PIP) Study. *Chest* 2000;117:1031-7.
18. Kumarasamy N, Vallabhaneni S, Flanigan TP, Meyer KH, Solomon S. Clinical profile of HIV in India. *Indian J Med Res* 2005;121:377-94.
19. Stansell JD, Osmond DH, Charlebois E, et al. Predictors of pneumocystis carinii pneumonia in HIV infected persons. *Am J Respir Crit Care Med* 1997;155:60-6.