

# Respiratory Complications in Human Immunodeficiency Virus Seropositive Patients in Correlation to CD4 Count: An Observational Cross-Sectional Study

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## Abstract

**Introduction:** Despite the advent and easy access of antiretroviral therapy (ART), human immunodeficiency virus (HIV) associated respiratory complications remains a significant cause of mortality and morbidity among HIV-seropositive individuals. CD4 count is an excellent indicator for developing opportunistic respiratory infections and complications.

**Materials and Methods:** We prospectively and cross sectionally studied the clinical, laboratorial, microscopical, and radiological parameters of 227 HIV-seropositive patients with respiratory complications at Government Medical College Hospital and ART Center over a period of 2 years with a view to identify the correlation of CD4 count and respiratory complication.

**Results:** Our study documented pulmonary tuberculosis (PTB) as the most common respiratory complication seen in 147 patients (64.76%) followed by bacterial pneumonia (BCP) in 51 patients (22.47%) followed by other fungal infections seen in 20 patients (8.81%). Pneumocystis pneumonia was seen in 7 patients (3.08%). Malignancy was seen in 2 patients (0.88%). PTB and BCP occurred at all CD4 count levels, but incidence increases in patients with lower CD4 counts.

**Conclusion:** There is a strong correlation between CD4 count and pattern of respiratory complications in HIV seropositive patients. Patients with CD4 count <200 cells/ $\mu$ L are more prone for respiratory complications. Hence, high level of clinical suspicion required for diagnosis of respiratory complications in HIV-infected individuals particularly with patients having CD4 count <200 cells/ $\mu$ L.

**Keywords:** CD4 count, Human immunodeficiency virus, Respiratory complications

## INTRODUCTION

In India first case of human immunodeficiency virus (HIV), infection was reported in Chennai in 1986.<sup>1</sup> Since then the incidence of HIV infection is increasing in Asia, particularly in the Indian subcontinent. India is in the epicenter of HIV pandemic.<sup>2</sup> The total number of people living with HIV/acquired immunodeficiency syndrome (AIDS) in India are estimated at 23.9 lakh in 2009.<sup>3</sup> Pulmonary complications have been one of the most common causes of morbidity and mortality since advent of AIDS. The opportunistic infections are caused by mycobacterial, bacterial, viral, fungal, parasitic pathogens. Each of these opportunistic infections has characteristic

clinical and radiographic presentation. CD4 cell count is an excellent indicator of an HIV-infected patient's risk of developing opportunistic pulmonary infections presumably because it reflects stage of HIV disease and degree of immunocompromise. Each of HIV-related respiratory illness typically develops at or below a characteristic CD4 cell count range.<sup>4</sup> Hence, knowledge of the CD4 count is extremely important in defining possible diagnosis and therapeutic plan. Pulmonary complications are also likely to vary according to geographical location, HIV risk factors, gender, and social habits of patients. Hence, present study is aimed at evaluating clinical profile of respiratory complications among HIV-seropositive patients in correlation to CD4 count levels. Knowledge of the pattern

of the pulmonary complications in HIV will help clinicians to develop faster diagnostic and therapeutic approach.

## MATERIALS AND METHODS

This is prospective observational cross-sectional study of 227 patients attending antiretroviral therapy center and outpatient department as well as inpatient department (both wards and intensive care unit) for a period of 2 years from January 2012 to December 2013 undertaken in tertiary care hospital in Department of Medicine, Government Medical College, Latur.

HIV seropositive patients irrespective of their antiretroviral treatment status above the age of 12 years and <60 years are included.

Patients known case of respiratory disorder such as asthma, chronic obstructive airway disease, and lung cancer. Patients known cases of any illness other than respiratory disease (cardiovascular disorder such as ischemic heart disease, myocardial infarction, hypertensive heart disease and neurological diseases such as meningitis, encephalitis, and HIV encephalopathy) Patients suffering from extra-pulmonary tuberculosis (PTB) such as abdominal tuberculosis, tuberculosis meningitis, tuberculosis pericardial effusion, tuberculosis lymphadenopathy, and HIV-seropositive female with pregnancy were excluded (Table 1).

CD4 count was done as part of the initial evaluation. Patients divided into three groups according to their CD4 count:

- 1 Patients having CD4 count >500 cells/ $\mu$ L
- 2 Patients having CD4 count 200-499 cells/ $\mu$ L
- 3 Patients having CD4 count <200 cells/ $\mu$ L.

Results compiled and statistically analyzed with Chi-square test and unpaired *t*-test.

## RESULTS

Of 227 patients, majority of patients belong to age group 31-40 accounting for 109 patients (48.02%) followed by 51 patients of age group 21-30 (22.47%). 40 patients were from age group 41-50 (17.62%). 10 (4.40%) and 17 patients (7.49%) were from age group 12-20 and 51-60, respectively. Of 227 patients 147 (64.76%) were males, and 80 patients (35.24%) were females.

Of 227 patients, 153 (67.40%) patients were from rural locality and 74 (32.60%) were from urban locality.

Of 227 patients, 157 patients were having CD4 count <200 cells/ $\mu$ L (69.16%) and 59 patients were having CD4

count between 200 and 499 cells/ $\mu$ L (25.99%). 11 patients were having CD4 count >500 cells/ $\mu$ L (4.85%) (Table 2).

Of 227 patients, fever (84.58%) and weight loss (79.30%) were the most common constitutional symptoms. Among cardinal respiratory symptoms, productive cough (79.7%) was the most common respiratory symptom followed by chest pain (74.01%) and dyspnea (62.56%). Hemoptysis was seen in (17.18%) patients.

Among 227 patients, 95 patients having consolidation on chest X-ray (41.85%), Hilar lymphadenopathy in 89 patients (39.21%) followed by fibrosis in 42 patients (18.50%) followed by pleural effusion in 38 patients (16.74%). Miliary mottling was present in 19 patients (8.37%). Cavitory lesion was seen in 21 patients (9.25%). Bilateral diffuse nodular opacities were seen in 10 patients (4.41%). Bilateral symmetric perihilar interstitial opacification was seen in 3 patients (1.32%).

Of 227 patients, PTB was the most common respiratory complication seen in 147 patients (64.76%) followed by bacterial pneumonia (BCP) in 51 patients (22.47%) followed by other fungal infections seen in 20 patients (8.81%). Pneumocystis pneumonia (PCP) was seen in 7 patients (3.08%). Malignancy seen in 2 patients (0.88%) (Table 3).

PTB is the most common respiratory complication in HIV-seropositive patients. Its incidence increases as CD4 count declined. Of 157 patients diagnosed to have PTB, 112 patients were having CD4 count <200 cells/ $\mu$ L, 33 patients were having CD4 count between 200 and 499 cells/ $\mu$ L, and 2 patients were having CD4 count >500 cells/ $\mu$ L. BCP seen in 16 patients having CD4 count <200 cells/ $\mu$ L and in 26 patients having CD4 count

**Table 1: Distribution of patients according to CD4 count (cells/ $\mu$ L) and diagnosis**

CD4 count	Diagnosis					Total
	PTB	BCP	Fungal	PCP	Malignancy	
>500	02	09	00	00	00	11
200-499	33	26	00	00	00	59
<200	112	16	20	07	2	157
Total	147	51	20	07	02	227

Test used is Chi-square test,  $\chi^2=58.4$ ,  $df=8$ ,  $P<0.05$ , Significant, BCP: Bacterial pneumonia, PTB: Pulmonary tuberculosis, PCP: Pneumocystis pneumonia

**Table 2: Distribution of patients according to their CD4 count (cells/ $\mu$ L)**

CD4 count	Number	Percentage
>500	11	4.85
200-499	59	25.99
<200	157	69.16
Total	227	100

**Table 3: Distribution of patients according to their diagnosis**

Diagnosis	Number (n=227)	Percentage
PTB	147	64.76
BCP	51	22.47
Fungal infections	20	8.81
PCP	07	3.08
Malignancy	02	0.88
Total	227	100

BCP: Bacterial pneumonia, PTB: Pulmonary tuberculosis, PCP: Pneumocystis pneumonia

between 200 and 499 cells/ $\mu$ L. 9 patients of BCP were having CD4 count  $>500$  cells/ $\mu$ L. All patients of PCP, fungal infections, and malignancy were having CD4 count  $<200$  cell/ $\mu$ L.

In patients with CD4 count  $>500$  cells/ $\mu$ L, 9 chest X-ray showed consolidation and 2 showed Hilar lymphadenopathy, 1 showed pleural effusion, and 1 showed other radiological sign. In patients with CD4 count 200-499 cells/ $\mu$ L, 32 chest X-ray showed consolidation, 8 X-ray showed fibrosis, 22 showed Hilar lymphadenopathy, 11 X-ray showed pleural effusion, and 9 showed other radiological signs. Among patients with CD4 count  $<200$  cells/ $\mu$ L, consolidation was seen in 54 X-ray, fibrosis in 34, Hilar lymphadenopathy in 65, miliary mottling in 19, pleural effusion in 26, and other signs in 24 X-ray. Mean CD4 count among total patients was 179.95 cells/ $\mu$ L and among males it was 180.99 cells/ $\mu$ L. Among female patients, mean CD4 count was 179.99 cells/ $\mu$ L.

Mean CD4 count among patients of tuberculosis was 152.12 cells/ $\mu$ L and among patients of BCP it was 325.88 cells/ $\mu$ L. Mean CD4 count was 99 cells/ $\mu$ L, 54.78 cells/ $\mu$ L and 55 cells/ $\mu$ L in patients of PCP, fungal infections and malignancy, respectively.

Mean CD4 count among sputum positive patient was 217.08 cells/ $\mu$ L.

Mean CD4 count among sputum negative patients was 165.37 cells/ $\mu$ L.

## DISCUSSION

In the present study, of 227 patients, 157 patients were having CD4 count  $<200$  cells/ $\mu$ L (69.16%) followed by CD4 count between 200 and 499 cells/ $\mu$ L was present in 59 patients (25.99%). CD4 count  $>500$  cells/ $\mu$ L was present in 11 patients (4.85%).<sup>5</sup> Fever (84.58%) and weight loss (79.30%) were the most common constitutional symptom and among cardinal respiratory symptoms productive cough (79.74%) was the most common

presenting chief complaint of the patients followed by chest pain (74.01%) and dyspnea (62.56%). Hemoptysis was seen in 39 patients (17.18%).<sup>5,6</sup> In the present study, of 227 patients, 95 patients (41.85%) showed consolidation on chest X-ray followed by Hilar lymphadenopathy seen in 89 patients (39.21%). Fibrosis was seen in 42 patients (18.50%) and pleural effusion in 38 patients (16.74%). Miliary mottling was present in 19 patients (8.37%). Other radiological signs including cavitory lesion present in 21 patients (9.25%), B/L diffuse nodular opacities in 10 patients (4.41%), B/L symmetric perihilar interstitial opacification in 3 patients (1.32%).<sup>7</sup>

Of 227 patients, 147 patients were diagnosed to have PTB (64.76 %) and BCP in 51 patients (22.47%). Clinicoradiological features of 7 patients were suggestive of PCP (3.08%). Fungal infections like pulmonary aspergillosis, cryptococcosis, etc., were found in 20 patients (8.81%). Malignancy found in 2 patients (0.88%).<sup>7-10</sup>

In PTB fever, chronic productive cough and weight loss were major chief complaints of patients. Hemoptysis was seen in lesser number of patients due to less number of fibrocavitory lesions. Of 147 patients of tuberculosis, 112 patients having CD4 count  $<200$  cells/ $\mu$ L and 200-499 cells/ $\mu$ L in 33 patients and  $>500$  cells/ $\mu$ L in 2 patients. In PTB patients with CD4 count  $>200$  cells/ $\mu$ L were having typical presentation with all the patients positive for sputum acid-fast bacilli (AFB) and more number of classical fibrocavitory lesion on chest X-ray. But in PTB patients with CD4 count  $<200$  cells/ $\mu$ L sputum positivity for AFB was found to be low this is due to less number of cavitory lesions. Atypical X-ray findings were more and less number of classical fibrocavitory lesion because chest X-ray findings of tuberculosis in HIV will depend on the level of immunosuppression, and most of patients in the present study had CD4 count  $<200$  cells/ $\mu$ L and hence more number of atypical findings.

In BCP most patients presented with fever, purulent sputum, chest pain, and dyspnea with characteristically showing unilateral, focal, segmental, or lobar consolidation on chest radiograph. Of 51 patients of BCP, CD4 count  $<200$  cells/ $\mu$ L seen in 16 patients and CD4 count between 200 and 499 cells/ $\mu$ L in 26 patients. CD4 count  $>500$  cells/ $\mu$ L was seen in 9 patients. The most common organism isolated on sputum for gram stain and cultures was *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* and *Haemophilus influenzae*. Patients with BCP having CD4 count  $<200$  cells/ $\mu$ L are often associated with bacteremia and sepsis. Methicillin-resistant *S. aureus* is more common HIV-infected individual particularly at lower CD4 cell counts.

Clinicoradiological correlation, sputum examination, and bronchoscopic examination of 7 patients were suggestive of PCP. All patients of PCP were having CD4 count <200 cells/ $\mu$ L. Although PCP is AIDS-defining illness incidence of PCP was found to be low in the present study as well as in other Indian studies. This may be due to the fact that lack of proper diagnostic utilities for PCP and extensive use of CO-TRIMOXAZOLE prophylaxis and predominance of other pulmonary disease like PTB.

In fungal infections, *Candida albicans* and *Candida tropicalis* were the most common organisms found. *C. albicans* and *C. tropicalis* were proved to be pathogens by assessing gram staining of sputum showing yeast like budding cells with pseudohyphae in presence of numerous polymorphonuclear leucocytes, obtaining them on repeated culture in pure growth and improvements of symptoms with antifungal. Pulmonary aspergillosis was seen in 3 patients. Cryptococcus neoformans found in 1 patient. In all patients of fungal infections, CD4 count was <200 cells/ $\mu$ L.

Malignancy found in 2 patients was Lymphoma with CD4 count <200 cells/ $\mu$ L.

In the present study, of 227 patients, 64 patients (39.19%) found positive for sputum AFB and 163 patients (71.81%) were sputum AFB negative.<sup>5</sup> In patients with CD4 count <200 cells/ $\mu$ L, 29 patients (45.31%) found positive for sputum AFB. In patients with CD4 count between 200 and 499 cells/ $\mu$ L, 33 patients found positive for sputum AFB. 2 patients with CD4 count >500 cells/ $\mu$ L were found positive for sputum for AFB.

Mean CD4 count among total patients was 179.95 cells/ $\mu$ L. Mean CD4 count among males was 180.99 cells/ $\mu$ L and females was 179.39 cells/ $\mu$ L.<sup>5</sup> Mean CD4 count among PTB patients was 152.12 cells/ $\mu$ L and among patients of BCP was 325.88 cells/ $\mu$ L. Mean CD4 count among fungal infections was 54.78 cells/ $\mu$ L and among PCP patients was 99 cells/ $\mu$ L. Mean CD4 count among patients of malignancy was 55 cells/ $\mu$ L. Hence, it shows that all respiratory complications in HIV patients are more common at lower CD4 counts.

Mean CD4 count among sputum positive patients was 217.08 cells/ $\mu$ L. Mean CD4 count among sputum negative patients was 165.37 cells/ $\mu$ L ( $P < 0.0001$ ). Hence, the sputum negativity is more common with lower CD4 counts.

In present study, 157 patients were having CD4 count <200 cells/ $\mu$ L (69.16%), 59 patients (25.99%) were having CD4 count between 200 and 499 cells/ $\mu$ L and

11 patients were having CD4 count >500cells/ $\mu$ L (4.85%). Majority of PTB occurred in patients with CD4 count <200 cells/ $\mu$ L. BCP commonly found in patients with CD4 count <500 cells/ $\mu$ L. PCP and fungal infections and Malignancy seen in patients having CD4 count <200 cells/ $\mu$ L. Mean CD4 count among all patients was 179.95 cells/ $\mu$ L.<sup>5,7,11</sup> HIV-seropositive individual and patient having CD4 count <200 cells/ $\mu$ L is 6 times more likely to develop an opportunistic infection compared to those with CD4 count >350 cells/ $\mu$ L.<sup>12</sup> There is significant statistical correlation between CD4 count and respiratory complications ( $P < 0.05$ ). Hence, it shows that patients having CD4 count <200 cells/ $\mu$ L are more prone to all respiratory complications and associated with more number of atypical X-ray findings and sputum negative for AFB. Hence, CD4 count has a major role in diagnosis and treatment of respiratory complications in HIV-seropositive individual.

PTB is the most common respiratory complication seen in HIV-seropositive patients (64.76%) followed by BCP (22.47%) and fungal infections (8.81%).

CD4 count and profile of respiratory complications correlated very well. Decrease in CD4 count is associated with an increase in a number of pulmonary complications. Majority of pulmonary complications were seen in patients having CD4 count <200 cells/ $\mu$ L.

## CONCLUSION

There is a strong correlation between CD4 count and pattern of respiratory complications in HIV-seropositive patients. Patients with CD4 count <200 cells/ $\mu$ L are more prone for respiratory complications. Hence, high level of clinical suspicion required for diagnosis of respiratory complications in HIV-infected individuals particularly with patients having CD4 count <200 cells/ $\mu$ L.

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