

Study to Assess the Spectrum of Clinical Manifestations of Respiratory System in Newly Diagnosed Human Immunodeficiency Virus Positive And AIDS Patients in Relation to CD 4 Cell Counts

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ABSTRACT

Background: To assess the relationship of clinical manifestations to CD4 counts.

Method: 200 HIV infected and AIDS patients were included in the study. After pre-test counseling, written informed consent was obtained for HIV testing from all the subjects. Present medical history was recorded, thorough clinical examination was performed and demographic details were recorded on a structured Performa. All patients were subjected to CD4 counts and were divided into three groups accordingly. The serum of patients was tested for Anti-HIV antibodies by ELISA.

Immunophenotyping of lymphocytes was carried out by 2 – color analysis on BDFACS count system. Statistical analysis was done using statistical software. Chi-square test was use to assess the relationships.

Results: Symptoms (Cough, expectoration, breathlessness) and abnormal positive findings on systemic examination of respiratory system were presented in significant number of

patients and these were significant in group 1 as compared to group 2 and group 3 ($p < 0.05$).

Key Words: HIV, CD 4 Cell Counts, Respiratory Disease.

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Article History:

Received: 24-07-2017, Revised: 29-08-2017, Accepted: 25-09-2017

Access this article online

Website: www.ijmrp.com	Quick Response code 
DOI: 10.21276/ijmrp.2017.3.5.038	

INTRODUCTION

The evaluation of respiratory symptoms in HIV-infected patients can be challenging for a number of reasons. Respiratory symptoms are a frequent complain among HIV-infected individuals and may be caused by a wide spectrum of illnesses. The spectrum of pulmonary illnesses in HIV-infected patients includes both HIV-related and non-HIV-related conditions. The HIV-associated pulmonary conditions include both opportunistic infections (OIs) and neoplasms. The OIs involve bacterial, mycobacterial, fungal, viral, and parasitic pathogens. Each of these OIs and neoplasms has a characteristic clinical and radiographic presentation. However, there can be considerable variation and overlap in these presentations. Therefore, no constellation of symptoms, physical examination findings, laboratory abnormalities, and chest radiographic findings are pathognomonic or specific for a particular disease. As a result, a definitive microbiologic or pathologic diagnosis is preferable to

empiric therapy whenever possible.¹ Patients with CD 4+ T cells level below certain thresholds are at higher risk of developing a variety of opportunistic diseases, particularly the infection and neoplasms that are AIDS defining illness.² CD4 cell count is an important investigation in the clinical evaluation of any patient with HIV infection, as it helps to decide the stage of HIV. It also assists in differential diagnosis and in making therapeutic decisions regarding antiretroviral treatment and prophylaxis against opportunistic infections.³ Serial CD4 cell counts have a prognostic significance and are used as markers for assessing progression from HIV infection to AIDS.⁴

Diagnostic tests include cultures from sputum and blood and from respiratory specimens obtained by invasive procedures such as bronchoscopy, thoracocentesis, computed tomography (CT) - guided transthoracic needle aspiration, thoracoscopy, mediastinoscopy, and open-lung biopsy.

METHODS

In this study 200 patients were taken and thorough clinical examination and investigation were done to assess the spectrum of clinical manifestation of respiratory system in newly diagnosed HIV positive and AIDS patients, we also assessed the relationship of clinical manifestations to CD4 cell counts in these patients.

HIV serology – the serum of patients were tested for anti-HIV antibodies by enzyme linked immunosorbent assay (ELISA). ELISA three kit test were used for confirmation of HIV infection - 1. SD BIOLINE, (HIV-1/2 3.0 Rapid test procedure), 2. HIV COMB Rapid test, 3. HIV TRIDOT Rapid test. These are rapid visual test for qualitative detection of antibodies to HIV 1 and HIV 2 in human serum/plasma.⁵

CD 4 Cell Count Estimations

Immunophenotyping of lymphocytes was carried out by 2-colour analysis on BD FACS count system (BECTON DICKINSON). Lymphocytes were stained according to the protocol suggested by the manufacturer.

Statistical Analysis

Patients with various clinical presentations were stratified into 3 groups of CD4 cell counts: <200, 200 – 500 and >500/ μ L and Univariate Analysis was done. Chi-square test was used to assess the relationship between the clinical statuses of patient with different CD4 cell counts.

The individuals were divided into three groups:

Group 1: Patients with HIV infection, symptomatic and CD4 cell counts <200/ μ L.

Group 2: Patients with HIV infection, symptomatic and CD4 cell counts 200-500/ μ L.

Group 3: Patients with HIV infection, symptomatic and CD4 cell counts >500/ μ L.

Patient who were on HAART or chemotherapy were excluded from the study.

Symptoms

Respiratory symptoms included cough, dyspnea, and pleuritic chest pain, either alone or in combination. Cough was nonproductive or productive (with purulent sputum, blood-streaked sputum, or even frank hemoptysis). Constitutional complaints such as fever, chills, night sweats, fatigue, anorexia, and weight loss was also present.

Signs

A complete physical examination, including vital signs, may provide important clues to the nature and severity of the disease. HIV-infected patients with pneumonia may be febrile, tachycardiac and tachypneic.

Evidence of wheezing in an HIV-infected patient who has a history of asthma suggests an asthma exacerbation, whereas findings of decreased breath sounds in a patient who has a long history of cigarette use may indicate emphysema. The remainder of the physical examination also may suggest an etiology for the respiratory symptoms, because many of the OIs and neoplasms that affect the lungs can also cause extrapulmonary or disseminated disease.

RESULTS AND DISCUSSION

Progressive quantitative and functional depression of CD4 lymphocytes and other immunological subsets make the patients more prone to a wide array of infectious and non-infectious complications.

There are clear associations between immunosuppression, as indicated by the CD4 cell count, and the risk of developing specific pulmonary infections. Acute pharyngitis, bronchitis, sinusitis, recurrent bacterial pneumonia, pulmonary tuberculosis and viral pneumonia are more common in patients with CD4 cell count <200/ μ L wherever PJP, disseminated TB, disseminated MAC, fungal pneumonia, CMV or HSV pneumonia are more common in CD4 cell count <200/ μ L.⁶

Our study showed that cough was most common symptom present in 58% of patients followed by expectoration (25%).^{7,8} We observed that the prevalence of cough was significantly more in severely immunocompromised (CD4 <200/ μ L) patient rather than mild to moderate immunocompromised (CD4 >200/ μ L). We also observed that advanced respiratory disease presenting as breathlessness was more common in patients who had profound immunosuppression (CD4 <200/ μ L).

Expectoration, as an evidence of active inflammatory response against the respiratory pathogen, was more common in the patient who had CD4 cell count between >200 to 500/ μ L as compared to patients with profound immunosuppression ($X^2=4.63, P<0.05$) (Table 1).

Table 1: Clinical manifestations related to respiratory system

S. No.	Parameters	Total No. (n,%)	Group I	Group II	Group III
			CD4<200/ μ L (n ₁ , %* % [#])	CD4 200-500/ μ L (n ₂ , %* % [#])	CD4>500/ μ L (n ₃ , %* % [#])
		N _T = 200	N _{<200} = 61	N ₂₀₀₋₅₀₀ = 92	N _{>500} = 47
	Symptoms				
1	Cough	116 (58)	53(45.68)(86.88)	50 (43.1) (54.34)	13(11.2)(27.65)
2	Expectoration	51 (25.5)	12 (23.5) (19.67)	33 (64.7)(35.86)	6(11.76)(12.76)
3	Hemoptysis	14 (7)	5 (35.7) (8.19)	7 (50) (7.6)	2 (14.28) (4.25)
4	Chest pain	8 (4)	3 (37.5) (4.9)	5 (62.5) (5.43)	0 (0) (0)
5	Breathlessness	24 (12)	17 (70.8)(27.86)	6 (25) (6.5)	1 (4.16) (2.12)
6	Nasal congestion	45 (22.5)	11(24.44)(18.03)	19(42.22)(20.65)	15 (33.3) (31.9)
	Systemic Examination				
7	Abnormal positive respiratory finding	84 (42)	36(42.85)(59.01)	41 (48.8) (44.56)	7 (8.3) (14.89)

Table 2: Significance of clinical manifestations in relation to CD4 cell counts

	Group 1 versus Group 2	Group 2 versus Group 3	Group 1 versus Group 3
Cough	P < 0.001, X ² = 17.62	P < 0.01, X ² = 8.94	P < 0.001, X ² = 39.00
Expectoration	P < 0.05, X ² = 4.63	P < 0.01, X ² = 8.22	P > 0.05, X ² = 0.91
Hemoptysis	P > 0.05	P > 0.05	P > 0.05
Chest pain	P > 0.05	P > 0.05	P > 0.05
Breathlessness	P < 0.001, X ² = 13.08	P > 0.05, X ² = 1.25	P < 0.001, X ² = 12.60
Nasal and pharyngeal congestion	P > 0.05	P > 0.05	P > 0.05
Abnormal respiratory finding on chest examination	P > 0.05, X ² = 3.06	P < 0.001, X ² = 12.11	P < 0.001, X ² = 21.50

Data analysis showed that most of the positive abnormal respiratory finding was present in moderate to severe immunocompromised patients (CD4 <500/μL).

The Pulmonary Complications of HIV Infection Study demonstrated that respiratory symptoms were common complain among HIV-infected individuals and are frequently increased as CD4 counts decline to <200/μL.⁹

Respiratory symptoms may result from a wide spectrum of pulmonary illnesses that includes both HIV-related and non HIV-related conditions. Because prompt diagnosis and institution of appropriate therapy are essential for successful treatment of many of these conditions, the initial focus of the evaluation of respiratory symptoms, frequently and appropriately placed on the diagnosis of a HIV-related OI or neoplasm.

Upper respiratory tracts (URIs) such as sinusitis, pharyngitis and acute bronchitis were more common cause of respiratory symptoms than Pneumocystis jiroveci pneumonia (PJP), bacterial pneumonia (including pulmonary tuberculosis) or pulmonary Kaposi sarcoma combined.¹⁰

These spectrum of pulmonary illnesses dominated by URIs and acute bronchitis in an outpatient based clinical setting clearly shift toward the opportunistic pneumonias in an inpatient or hospital based clinical setting and it shift toward PJP in an intensive care unit based clinical setting.^{11,12} Therefore, the diagnostic approach to the evaluation of the respiratory symptoms in an HIV-infected patient must take all these factors into consideration.

In the current era of combination antiretroviral therapy, the frequency of HIV associated OIs and neoplasm has decreased.^{13,14} HIV infection appears to be an independent risk factor for COPD and PAH.¹⁵

The CD4 cell count is an excellent indicator of a HIV-infected patient's risk of developing a specific OI or neoplasm, presumably because it reflects the stage of HIV disease and degree of immunocompromised state. Each of the HIV-related illnesses typically develops at or below a characteristic CD4 cell count range and uncommonly or rarely occurs above these ranges (Table 2). As the CD4 cell count declines, the incidence of many of these diseases increase. As the CD4 cell count decrease to <500 cell/μL, episodes of bacterial pneumonia may be recurrent and infection of mycobacteria other than M. tuberculosis (e.g. M. kansasii) may occur.^{16,17}

At a CD4 cell count of <200/μL, bacterial pneumonia is often accompanied by bacteremia and sepsis, and M. tuberculosis infection is often extrapulmonary or disseminated. In addition, PJP and pneumonia caused by Cryptococcus neoformans become significant considerations.

At CD4 cell count of <50/μL, respiratory diseases caused by endemic fungi (e.g. Histoplasma capsulatum, Coccidioides immitis), certain viruses (most common - Cytomegalovirus), Mycobacteria (Mycobacterium avium complex), and nonendemic fungi (e.g. Aspergillus spp.) occur because each of the OIs typically develops at or below a characteristic CD4 cell count range, so knowledge of a HIV-infected patient's CD4 cell count can be extremely useful in defining the possible diagnosis. For example, for a HIV infected patient whose CD4 cell count is significantly high >200 cells/μL, bacterial pneumonia (possibly TB, depending on the demography) should be consider for the differential diagnosis rather than PJP. The Centers for Disease Control and Prevention's Adult and Adolescent Spectrum of HIV Disease Project has provided statistics for the conditions which are more common with a particular CD4 cell count range.¹⁸

The vast majority (>80%) of bacterial pneumonias and pulmonary tuberculosis occurred in subjects with a CD4 cell count of <400/μL. Therefore, both of the disease should be considered at any CD4 cell count but are more common when the count is <400/μL.

Knowledge of the CD4 cell count is useful in narrowing the differential diagnosis, and knowledge of the relative frequencies of these pulmonary diseases can be useful in ranking potential diagnosis and suggesting a diagnostic and therapeutic plan. For example, if a HIV infected patient presents with respiratory symptoms and CD4 cell count of >200/μL, PJP is unlikely, while bacterial pneumonia is more likely diagnosis than pulmonary tuberculosis. In that case, the diagnostic plan should include sputum and blood cultures for bacteria, and therapy probably should target the most common bacterial pathogens.

ACKNOWLEDGEMENT

I am very grateful to Dr H C Badjatya, Head of Unit, department of medicine, JLNMC, Ajmer, for guiding me and also thankful to all the staff of ART center, Ajmer to support me in conducting this study.

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Source of Support: Nil.

Conflict of Interest: None Declared.

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Cite this article as: Dharmendra K Kanwaria, Navendra K Gupta, Manish Singhal, K C Nayak. Study to Assess the Spectrum of Clinical Manifestations of Respiratory System in Newly Diagnosed Human Immunodeficiency Virus Positive And AIDS Patients in Relation to CD 4 Cell Counts. *Int J Med Res Prof.* 2017 Sept; 3(5):192-95. DOI:10.21276/ijmrp.2017.3.5.038