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**Research Article**

# HIV/AIDS-tuberculosis (pulmonary and extra pulmonary) co-infection: CD4 correlation

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## ABSTRACT

**Background:** AIDS is the leading cause of death among people 15-59 years old in low income countries. Worldwide, approximately one-third of all AIDS-related deaths are associated with TB. TB is the primary cause of death for 10-15% of patients with HIV infection. So the present study was conducted to find the correlation between sputum positivity and CD4 cell count in patients with HIV/AIDS-Tuberculosis co-infection.
**Methods:** The present study was a retrospective hospital based study of patients with HIV/AIDS-Tuberculosis co-infection, attending ART centre, department of medicine, Osmania general hospital, Hyderabad, Telangana, India between November 2014 to September 2015. Data included clinical profile, complete blood picture, renal and liver function tests, sputum microscopy and C/S and chest X-Ray and others as and when required.
**Results:** We included 180 HIV/AIDS infected patients on ART with tuberculosis (TB) co-infection. Out of 180 patients, 132 were males and 48 were females. Among male's ≥40 (51.51%) year's age group and among females 30-39 (56.25%) year's age group was the most commonly affected. Out of 180 cases 60 were sputum positive. 60 sputum negative pulmonary tuberculosis and 60 were extra pulmonary TB. CD4 cell count was <200/mm$^3$ in 36 (60%) of sputum positive TB, 43 (71.7%) of sputum negative pulmonary TB & 39 (65%) of extra pulmonary TB patients. CD4 cell count was 200-400/mm$^3$ in 16(26.7%) of sputum positive pulmonary TB, 13 (21.7%) of sputum negative TB and 19 (31.7%) of extra pulmonary TB patients. CD4 cell count was >400/mm$^3$ in 8 (13.3%) of sputum positive pulmonary TB, 4 (6.6%) of sputum negative pulmonary TB and 2 (3.3%) of extra pulmonary TB patients.
**Conclusions:** Present study concludes that male sex and age group >30 years were the commonly affected population. All forms of tuberculosis were common when CD4 count was <200 cells/mm$^3$. The sputum negativity was higher with lower CD4 counts.

**Keywords:** HIV, Tuberculosis, CD4 count, Extra pulmonary tuberculosis, Opportunistic infection

## INTRODUCTION

The first cases of AIDS were described in the USA in 1981 and by 1985, HIV infection had been identified in every region of the world.[1-3] Analysis of phylogenetic sequences from human and related ape viruses suggests that HIV originated in Central Africa and may have first been transmitted to humans around 1930.[4] In the short time since then, HIV has reduced life expectancy, slowed economic growth and orphaned (loss of one or both parents) over 18 million children.[5] Prior to recent expansions in access to HIV treatment, AIDS was the leading cause of death among people 15-59 years old in low income countries (especially Sub-Saharan Africa);

fortunately, recent reports suggest some encouraging reversals of these trends.[6-7]

Worldwide, approximately one-third of all AIDS-related deaths are associated with TB, and TB is the primary cause of death for 10-15% of patients with HIV infection. Approximately 60-80% of HIV-infected patients with TB have pulmonary disease, and 30-40% has extra pulmonary disese.[8] The incidence of extra pulmonary features tends to increase with advancing immunosuppression in HIV-infected persons. In patients with relatively high CD4+Tcell counts, the typical pattern of pulmonary reactivation occurs and patients present with fever, cough, dyspnea on exertion, weight loss, night sweats, and a chest X-ray revealing cavitary apical disease of the upper lobes. In patients with lower CD4+T cell counts, disseminated disease is more common.[8]

The commonest manifestations of extra pulmonary tuberculosis are superficial lymphadenitis, genitourinary disease, pleural disease, miliary disease, bone and joint disease and abscesses of the soft tissues. Pericardial disease is of particular importance in HIV-infected patients in the developing world and mycobacterial bacteraemia may be detected in most HIV-infected patients with tuberculosis.[9]

## METHODS

It was as a retrospective hospital based study. Data of HIV/AIDS infected patients on ART with tuberculosis co-infection attending ART Centre, Department of medicine, Osmania general hospital between November 2014 to September 2015 was collected. 180 patients were included in the study.

### *Investigations*

Complete blood picture, serum creatinine, blood urea, serum electrolytes, liver function tests, sputum for acid fast *bacilli* smear, chest radiography, CD4 cell count, fine needle aspiration and biopsy (if necessary), magnetic resonance imaging (if necessary), computed tomography (if necessary), colonoscopy (if necessary).

## RESULTS

A total of 180 patients were included in the study. As shown in Table 1 there were 132 (73.3%) male and 48 (26.7%) female patients. The age distribution is shown in Table1. Among males ≥40 (51.51%) years age group and among females 30-39 (56.25%) years age group was the most commonly affected.

Out of 180 cases 60 were sputum positive, 60 were sputum negative pulmonary tuberculosis and 60 had extra pulmonary disease.

In the present study among sputum positive cases mean age was 39 years with mean CD4 count of 183 cells/mm$^3$, in sputum negative cases the mean age was 40 years with mean CD4 count of 176 cells/ mm$^3$ and in extra pulmonary tuberculosis the mean age was 42 years with mean CD4 count of 168 cells/mm$^3$.

**Table 1: Age and sex distribution of patients.**

| Age group (years) | Male (n,%) | Female (n,%) | Total (n,%) |
|---|---|---|---|
| <20 | 01 (0.76%) | 0 (0%) | 01 (0.55%) |
| 20-29 | 24 (18.18%) | 8 (16.67%) | 32 (17.78%) |
| 30-39 | 39 (29.55%) | 27 (56.25%) | 66 (36.67%) |
| ≥40 | 68 (51.51%) | 13 (27.08%) | 81 (45%) |
| Total | 132 | 48 | 180 (100%) |

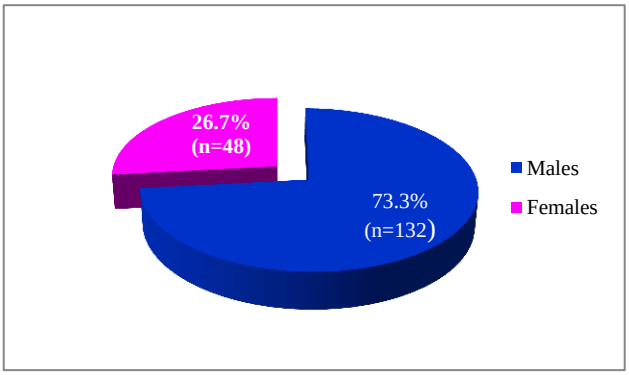


**Figure 1: Sex distribution.**

The co-relation of CD4 cell count with different forms of tuberculosis are shown in Table 2-4 and Figure 2.

**Table 2: CD4 cell count in smear positive pulmonary tuberculosis.**

| Gender | CD4<200 | CD4 between 200-400 | CD4>400 | Total |
|---|---|---|---|---|
| Female | 8(13. 3%) | 3(5%) | 1(1.7%) | 12(20%) |
| Male | 28(46.7%) | 13(21.7%) | 7(11.6%) | 48(80%) |
| Total | 36(60%) | 16(26.7%) | 8(13.3%) | 60(100%) |

**Table 3: CD4 cell count in smear negative pulmonary tuberculosis.**

| Gender | CD4<200 | CD4 between 200-400 | CD4>400 | Total |
|---|---|---|---|---|
| Female | 9(15%) | 2(3.3%) | 1(1.7%) | 12(20%) |
| Male | 34(56.7%) | 11(18.3%) | 3(5%) | 48(80%) |
| Total | 43(71.7%) | 13(21.7%) | 4(6.6%) | 60(100%) |

**Table 4: CD4 cell count in extra pulmonary tuberculosis.**

| Gender | CD4<200 | CD4 between 200-400 | CD4>400 | Total |
|---|---|---|---|---|
| Female | 17(28.3%) | 6(10%) | 1(1.7%) | 24(40%) |
| Male | 22(36.7%) | 13(21.7%) | 1(1.6%) | 36(60%) |
| Total | 39(65%) | 19(31.7%) | 2(3.3%) | 60 (100%) |

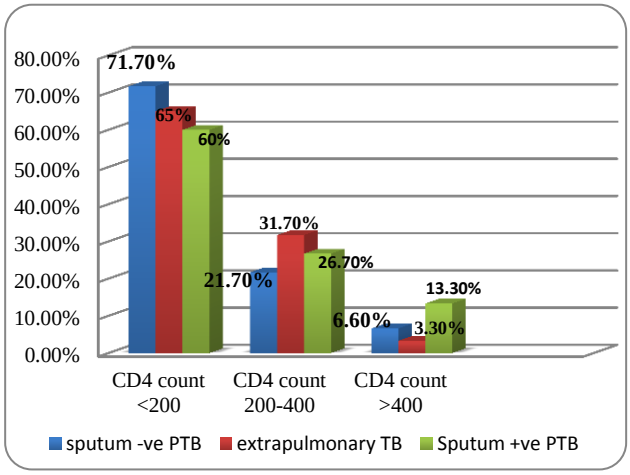


**Figure 2: HIV/AIDS-TB co-infection correlation with CD4 count.**

## DISCUSSION

The clinical features of tuberculosis in the HIV-positive patient depend on whether tuberculosis is developing early or late in the course of HIV infection.[10-12] Tuberculosis tends to occur earlier in the course of HIV infection and in this situation the clinical, radiological and bacteriological findings do not differ substantially from those found in HIV-negative patients. The disease is predominantly pulmonary, located in the upper lobes and cavitation occurs. Tuberculin tests are usually positive and sputum smear positivity is not decreased. When tuberculosis occurs later in the course of HIV infection or in patients with AIDS the features are more often atypical: pulmonary disease may occur in atypical sites, e.g. lower zone or diffuse consolidation, mediastinal adenopathy is more common and involvement of extra pulmonary sites such as brain, pericardium, bones and the gastrointestinal tract is found.[13,14] Cavitation of pulmonary lesions and tuberculin positivity are less common. Sputum smear negativity may be more common.[15]

Tuberculosis is the most common opportunistic infection in HIV/AIDS and is the most common cause of death in HIV/AIDS patients. Early diagnosis and treatment can decrease the mortality and morbidity. HIV enters the body when an individual comes in contact with infected blood, semen and/or vaginal secretions. The CD4 receptor is the principal target site for HIV.[16] A normal CD4 count in a healthy, HIV-negative adult can vary but is usually between 500 and 1500 CD4 cells/mm$^3$ (though it may be lower in some people). Opportunistic infections (OIs) may serve as indicators of underlying HIV infection. Mortality among HIV-infected individuals is due to improper awareness and consequent poor clinical management of OIs. HIV load increases in the presence of on-going OIs, thus accelerating progression to clinical acquired immunodeficiency syndrome (AIDS). The incidence of OIs range from 10.7 to 69.7/100 patient years.

Among 28 OIs- tuberculosis (65%), candidiasis (57.5%) and diarrhoeal diseases (40%) are the most common OIs found in Indian patients[17].

According to an estimate of World Health Organisation (WHO), TB has become one of the leading causes of death among HIV infected persons.[18]

TB is the most common treatable HIV-related disease and a leading killer of people living with HIV/AIDS (PLWHA). In India, there were an estimated 5.134 million PLWHA at the end of 2004.[19,20]

Tuberculosis can occur at any CD4 cell count. Pulmonary tuberculosis is more common at CD4 counts between 200-500/microL. Miliary and extra pulmonary tuberculosis at less than 200 cells/microL. MAC at less than 50 cells/microL.[21]

HIV infected smear positive patients tend to excrete significantly fewer organisms per ml of sputum than HIV-negative patients which can lead to AFB being missed if the appropriate number of sputum samples as well as high power fields is not examined by microscopy.[22]

The sputum negativity tends to increase as the HIV disease and immune suppression progresses. Severe immune suppression is defined as CD4 cells <200/microL.[23]

### *Prevention of tuberculosis*

TB is a major cause of death among people living with HIV/ AIDS and may lead to increased HIV disease progression.[1,24,25] TB is more common in those with advanced immune suppression but can present across a wide spectrum of CD4 counts.[1,26] Randomized controlled studies have shown that a 6-month course of isoniazid reduces the risk of active disease in HIV-infected individuals with latent infection with *Mycobacterium tuberculosis* indicated by a positive tuberculin skin test (TST) in the absence of active TB disease.[1,27] The TST reaction does not distinguish between active and latent infection and also does not have optimal sensitivity and specificity. Although in several trials primary prophylaxis was shown to decrease the incidence of active TB in

TST-positive, HIV-infected individuals, in only one placebo-controlled trial conducted in Haiti prior to the availability of ART was isoniazid prophylaxis associated with increased survival. WHO recommends that HIV/AIDS programmes provide isoniazid preventative therapy as part of the package of care for people living with HIV/AIDS. However, exclusion of active tuberculosis is critically important before chemoprophylaxis is started. The recommended regimen is isoniazid 5 mg/kg up to a maximum of 300 mg daily for 6-9 months, during which time patients should be clinically monitored for toxicity and for active tuberculosis.[1,28]

***Treatment***

Patients were treated based on RNTCP and NACO guidelines. Anti-tuberculosis therapy (ATT) were administered according to the directly observed treatment-short course (DOTS) regimen. Institution of highly active anti-retroviral therapy (HAART) was done 10-14 days after institution of ATT in patients with CD4 counts less than 200 cells/$mm^3$. In patients with CD4 counts over 200 cells/$mm^3$ HAART was commenced 2-8 weeks after the institution of ATT. As rifampicin is known to enhance the metabolism of protease inhibitors and nevirapine, efavirenz based antiretroviral therapy (ART) was recommended while patients are on rifampin.

In comparison with previous study conducted by Siddeswari R et al from the same institute the CD4 count was correlating to the present study. CD4 cell count <200 microL in sputum positive cases 60% (present study) versus 52%, in sputum negative pulmonary tuberculosis 71.1% (present study) versus 72%, in extra pulmonary tuberculosis in 65% (present study) versus 66%.[29]

## CONCLUSION

Present study concludes that male sex and age group >30 years were the commonly affected population. CD4 cell count was <200/$mm^3$ in 36 (60%) of sputum positive PTB, 43 (71.7%) of sputum negative pulmonary TB & 39 (65%) of extra pulmonary TB patients. CD4 cell count was 200-400/$mm^3$ in 16 (26.7%) of sputum positive pulmonary TB, 13(21.7%) of sputum negative pulmonary TB and 19 (31.7%) of extra pulmonary TB patients. CD4 cell count was >400/$mm^3$ in 8 (13.3%) of sputum positive pulmonary TB, 4 (6.6%) of sputum negative pulmonary TB & 2 (3.3%) of extra pulmonary TB patients.

In the present study among sputum positive cases mean age was 39 years with mean CD4 count of 183 cells/$mm^3$, in sputum negative cases the mean age was 40years with mean CD4 count of 176 cells/ $mm^3$ and in extra pulmonary tuberculosis the mean age was 42 years with mean CD4 count of 168 cells/$mm^3$.

Even though sputum positivity did not correlate well with CD4 cell count, sputum negativity increased with decrease in CD4 cell count. With arbitrary cut off of CD4 cell count of <200 microL, the incidence of extra pulmonary tuberculosis was higher.

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## REFERENCES

1. Philip J. Peters, Barbara J. Marston, Kevin M. De Cock; SECTION 5 Viral Infections Chapter 9 HIV Epidemiology in the Tropics.Manson's Tropical Diseases,23rd edition, Elsevier Limited;Pg 68-78.
2. Pneumocystis pneumonia – Los Angeles. MMWR 1981;30:250–2.
3. UNAIDS. 2006 Report on the global AIDS epidemic. Available at http://data.unaids.org/ pub/ GlobalReport/2006/2006_grexecutivesummary_en.pdf.Last accessed on 18th October 2015.
4. Korber B, Muldoon M, Theiler J, Gao F, Gupta R, Lapedes A. Timing the ancestor of the HIV-1 pandemic strains. Science. 2000;288:1789-96.
5. UNAIDS. Report on the global HIV/AIDS epidemic 2008.Available: http://www. unaids.org/ en/data analysis/epidemiology/2008_report_on_the_global_ aids_epidemic/ (Accessed 5 May 2011).
6. World Health Organization. The global burden of disease: 2004 update. Available: http://www.who.int/healthinfo/global_burden_disease/ 2004_report_update/en/index.html (Last accessed 18th october 2015).
7. Dlodlo RA, Fujiwara PI, Hwalima ZE, Mungofa S, Harries AD. Adult mortality in the cities of Bulawayo and Harare, Zimbabwe: 1979-2008. Journal of the International AIDS Society. 2011;14(Suppl 1):S2.
8. Fauci AS, Lane HC. Human Immuno deficiency Virus Disease: AIDS and Related Disorders; Harrison's Principles of Intermal Medicine 19 edition. 2015;226:1215-85.
9. Seaton RA. Extra-pulmonary tuberculosis, Crofton and Douglas's Respiratory diseases. Fifth Edition. 2000;18:535-52.
10. Leitch AG. Pulmonary Tuberculosis: Clinical Features, Ch7; Crofton and Douglas's Respiratory Diseases. fifth edition. 2000;11:7:507-27.
11. Handwerger S, Mildvan D, Senie R, McKinley FW. Tuberculosis and the acquired immunodeficiency syndrome at a New York City Hospital, 1978–1985. Chest. 1987;91:176-80.
12. Hopewell PC. Reichman LB et al., Tuberculosis and infection with the human immunodeficiency virus. In New York, Tuberculosis.1993:369.
13. Pastores SM, Naidich DP, Aranda CP, McGuinnes G, Rom WN. Intrathoracic adenopathy associated with pulmonary tuberculosis in patients with Human Immunodeficiency Virus infection. Chest. 1993;103:1433-7.

14. Lucas SB, De Cock KM, Hounnou A, Peacock C, Diomande M, Hondé M, Beaumel A, et al. Contribution of tuberculosis to slim disease in Africa. Br Med J. 1994;308:1531-3.
15. Elliott AM, Namaambo B, Allen BW, Luo N, Hayes RJ, Pobee JO, et al. Negative sputum smear results in HIV positive patients with pulmonary tuberculosis in Lusaka, Zambia. Tubercle Lung Dis. 1993;74(3):191-4.
16. Ravi V, Desai A. HIV and AIDS, API textbook of medicine. 9E,16(2):1014-16.
17. Edwin N, Mathai D. Oppurtunistic infections, HIV and AIDS, API textbook of medicine, 9E, 16(7):1032-35.
18. World Health Organisation. Tuberculosis facts 2007.Available from http://www.cdc.gov/ hivtb.htm (Last Accessed on 2008 Jan 14).
19. National AIDS Control Organisation (NACO) – Estimation of HIV infection in India. Available at http:// www.nacoonline.org/ facts_hivestimates.htm (Last accessed on 18th October 2015).
20. AIDS Profile:India. Available at http://www.census.gov/ ipc/ www/hivctry.html. (Last accessed on 18th October 2015).
21. Beck JS, Potts RC, Kardjito T, Grange JM. T4 Lymphopenia in patients with active pulmonary tuberculosis. Clin Exp Immunl. 1985:60:49-50.
22. Singhal M, Banavalikar JN, Sharma S, Saha K. Peripheral blood T lymphocytes subpopulation in patients with tuberculosis and the effect of chemotherapy. Tubercle. 1989:70(3):171-8.
23. Turret GS, Telzak EE. Normalisation of CD4+ T-lymphocyte depletion in patients without HIV infection treated for tuberculosis. Chest. 1994:105:1335-7.
24. Lucas SB, Hounnou A, Peacock C, Beaumel A, Djomand G, N'Gbichi JM, et al. The mortality and pathology of HIV infection in a West African city. AIDS. 1993;7:1569-79.
25. Badri M, Ehrlich R, Wood R, Pulerwitz T, Maartens G. Association between tuberculosis and HIV disease progression in a high tuberculosis prevalence area. Int J Tuberc Lung Dis. 2001;5(3):225-32.
26. Wood R, Maartens G, Lombard CJ. Risk factors for developing tuberculosis in HIV-1 infected adults from communities with a low or very high incidence of tuberculosis. AIDS. 2000;23(1):75-80.
27. Wilkinson D. Drugs for preventing tuberculosis in HIV infected persons. Cochrane Database Systematic Review 2000;(4):CD000171.
28. Pape JW, Jean SS, Ho JL, Hafner A, Johnson WD Jr. Effect of isoniazid prophylaxis on incidence of active tuberculosis and progression of HIV infection. Lancet. 1993;342:268-72.
29. Siddeswari R, Sudarsi B, Sanjeev, Suryanarayana B, Manohar S, Abhilash. HIV/Aids-Tuberculosis (pulmonary and extra pulmonary) co-infection: sputum positivity and Cd4 Correlation. International journal of scientific and research publications. 2015;5(2):1-4.


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