The CD4 cell count recovery in HIV and tuberculosis co-infected patients versus tuberculosis uninfected HIV patients in a tertiary care Hospital

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Abstract: Introduction: Human Immunodeficiency Virus (HIV) infected patients have an increased risk of developing tuberculosis (TB) due to a loss of cell mediated immunity, along with a quantitative decline in circulating CD4 lymphocytes and tuberculosis occurs sooner than other opportunistic infections. The dual (HIV/TB) infection compared with CD4 matched cohort of TB uninfected HIV patients. We sought to test the hypothesis; TB additionally contributes to reduction in CD4 count in HIV/TB co-infected patients and leads to greater improvement in count following treatment as compared to CD4 matched TB uninfected individuals. Material and Methods: This is a retrospective cohort study. We studied the change in CD4 cell count in two groups of patients, those with CD4 cell count >200 cells/mm³ (Group 1) and < 200 cells/mm³ (Group 2) at presentation. In each group the change in CD4 cell count in dually infected patients following six months anti-tuberculosis therapy (ATT) and anti-retroviral therapy (ART) was compared to cohort of CD4 matched TB uninfected patients only on ART. Results: In group1 (156 cases) dually infected patients CD4 count improved from 250 to 450 cells/mm³ and in TB uninfected (control) patients the change was from 260 to 422 cells/mm³. In group 2 (180 cases) dually infected subjects count improved from 150 to 355 cells/mm³, where as in TB uninfected (control) patients improvement was from 170 to 330 cells/mm³. Conclusion: Greater improvement in CD4 count with ATT and ART in dually infected patients, it may suggests that TB additionally influences the reduction of CD4 count in HIV patients.

Keywords: Anti-tuberculosis therapy, anti-retroviral therapy and CD4 cell lymphocyte of cryptosporidiosis in HIV infected patients and simple method modified ZN staining can detect oocyst in stool sample.

Introduction: Tuberculosis (TB) is the leading cause of death in HIV patients. The mortality of TB in HIV patients is two to four folds more than in HIV negative patients. TB is the cause of death in one out of three PLWHA (people living with HIV/AIDS). TB also accelerates HIV infection by increasing viral load by five to seven folds. TB is not only the most common opportunistic infection but also increases the risk of other opportunistic infections1,2,3. There is clinical and experimental evidence suggesting that active TB accelerate the course of HIV disease4. TB causes a continuous cellular activation and irregularities in cytokines and permissive for HIV replication5. The key components of the immune response in TB include T lymphocytes and alveolar macrophages. The T helper type 1 subclass is the major effector cell in cellular immunity of TB or the ‘policeman’ of TB control in the lung resulting in dissemination of Mycobacterium tuberculosis6. The study showed improvement in CD4 count with ATT and ART in patients presenting with dual infection as compared to CD4 matched cohort of TB uninfected HIV patients initiated on ART4. One study hypothesized that TB infection contributes to additional reduction in CD4 cell count in HIV patients presenting with dual infection4. There would be greater improvement in CD4 count following ATT and ART when compared to TB uninfected HIV patients initiated only on ART4. They tested this hypothesis in a retrospective cohort study design4. We studied the change in CD4 count in dually infected subjects following ATT and ART as compared with a CD4 matched cohort of HIV patients without TB.

Material and Methods: This retrospective study was conducted for a period of three years (January 2009 to December 2011) at our tertiary care Hospital. The patients’ blood was tested for HIV antibodies by NACO (New Delhi) approved three different rapid immunochromatography test kits, following its testing guidelines6. CD4/CD8 cell count and their ratio by two color immuno phenotyping on the single platform fluorescence activated cell sorting (FACS) count system (Becton Dickinson Pvt. Ltd Company, signature tower B, south city 1, Gurgaon, Haryana, India) using fluorochrome labeled monoclonal antibodies to CD4 and CD8 T cells, strictly following manufactures instructions. FACS count protocol software versions 1.2(3/95), 1.3(2/00) and 1.4(4/02) [Becton Dickinson] were used for data acquisition and analysis. The diagnosis of pulmonary tuberculosis during screening, three sputum samples per patient were collected and stained by using the Ziehl-Neelsen (ZN) technique. The smears were examined using
Patients in group 1B and 2B were also identified from the same clinic and details were collected from the case files and registers. The baseline characteristics of patients including age, gender, weight, type of TB and CD4 count at presentation were noted from the case files and registers. Patients in group 1A and 2A received ATT and ART and CD4 count matched control groups without TB infection. In group 1A, mean CD4 count improved from 250 to 450 cells/mm$^3$ and mean weight changed from 50 to 57 Kg. In group 1B, mean CD4 count improved from 260 to 422 cells/mm$^3$ and mean weight improved from 52 to 60 Kg. In group 2A and 2B, there were 180 patients each. The baseline characteristics were comparable between the groups. Here also there were more male patients in the co-infection group. In group 2A, mean CD4 count improved from 150 to 330 cells/mm$^3$ and mean weight changed from 52 to 59 Kg. When compared between the groups there were more increment in mean CD4 count in group 1A and 2A.

### Results:

In group 1A and 1B, there were a total of 156 patients each. The baseline characteristics were comparable between the groups (Table 1).

### Discussion:

In this retrospective cohort study we compared the change in CD4 count following ATT and ART in HIV/TB co-infected patients with a CD4 matched cohort of TB uninfected patients initiated on ART. There was greater improvement in CD4 count in patients with dual infection. One article had published regarding the similar study, as analyzing CD4 cell recovery in HIV/TB co-infection compared with a CD4 cell count matched cohort of HIV patients uninfected with TB. Additional increment in CD4 count in patients with co-infection following treatment suggests that CD4 suppression at the onset of TB may be the direct evidence of *Mycobacterium tuberculosis* growth. Inflammation and interaction between TB and HIV have additional effect on CD4 cells as compared to HIV alone. CD4 lymphocyte depletion is known to occur in TB patients not infected by HIV and become normalized following ATT. In series of 85 patients with TB not infected by HIV, 37 showed low CD4 cell count and 48 had normal count. Disease
severity was associated with greater depression in total lymphocyte as well as CD4 count. CD4:CD8 ratio remained normal in 90% of patients with tuberculosis. Previous studies carried out in dually infected subjects not receiving ART show variable results with regard to change in CD4 count following ATT 12,13,14,15. In a prospective study conducted in Chennai, dually infected subjects treated with ATT and not receiving ART showed no change in CD4 count but CD4 percentage decreased 4,12. In South African patients with dual infection not receiving ART, median CD4 count improved from 186 cells/mm³ at baseline to 239cells/mm³ after six months of ATT but the change was not statistically significant 13. In the prospective study by KalouM, et al, CD4 count changed from 393 cells/mm³ at baseline to 379 cells/mm³ after 12 months of follow-up 14. In the study by Elliott AM, et al in HIV patients with pleural TB, CD4 count improved following ATT but did not reach statistical significance 15. There are few studies comparing the change in CD4 count before and after ATT in dually infected subjects in comparison to TB patients not infected by HIV 4. In the study by Mortin DJ, et al, CD4 count increased significantly in both cohorts of HIV/TB group and TB group following routine ATT 16. But the Tai study showed contrary results 17. The CD4 cell count among non HIV patients was 510 cells/mm³ and increased to 867 cells/mm³ after six months of therapy. Among HIV infected patients, the CD4 count cell was 64cells/mm³ and decreased to35 cells/mm³ after six months of therapy. But the small sample size was a major limitation of the Thai study. The improvement in CD4 count following ATT and ART and no change following ART alone may indicate a role for immune reconstitution following ART especially in patients with very low CD4 count 4,17. Our retrospective study provides some evidence in the clinical setting that TB additionally influences the reduction in CD4 cell count in HIV patients.

**Conclusion:**
In HIV/TB co-infected individuals TB additionally contribute to reduction in CD4 counts as evidenced by greater improvement in CD4 counts in these patients following six months of treatment with ATT and ART when compared to CD4 cell count matched cohort of TB uninfected HIV patients on ART alone.

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**References:**
3. NACOonline.org, http://www.nacoonline.org

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