



## EVALUATION OF CD4 T-CELL COUNTS IN HIV/TB COINFECTED PATIENTS BEFORE AND AFTER ANTI-TUBERCULAR TREATMENT.

### Microbiology

**Dr. Ghanta Naga Sai Snigdha** Postgraduate ( MD Microbiology) Department of Microbiology, Rangaraya Medical College, GGH Campus, Kakinada-E.G. District, Andhra Pradesh, India.

**Dr. G. Ratna Kumari\*** Professor, Department of Microbiology, Rangaraya Medical College, GGH Campus, Kakinada-E.G. District, Andhra Pradesh, India. \*Corresponding author

### ABSTRACT

Tuberculosis (TB) is a common coinfection in Human Immunodeficiency virus (HIV) infected patients worldwide, especially in developing countries. This coinfection has dreadful social and economic impact across the globe. A decrease in CD4 T-cell counts in HIV-TB coinfection leads to increase in morbidity and mortality. This retrospective study was conducted to evaluate CD4 T-cell counts in coinfecting patients of HIV and TB before and after anti tubercular treatment (ATT). Of the 186 coinfecting patients observed, 160 had pulmonary tuberculosis (PTB) and 26 had extra-pulmonary tuberculosis (EPTB). The mean CD4 counts before ATT in PTB patients is 266 cells/ $\mu$ l and EPTB patients is 248 cells/ $\mu$ l and after the completion of ATT in PTB is 332 cells/ $\mu$ l and 397 cells/ $\mu$ l in EPTB patients. There was statistically significant increase in CD4 T-cell counts in both PTB and EPTB cases coinfecting with HIV after ATT.

### KEYWORDS

CD4 T-cell count, HIV-TB coinfection, ATT.

### INTRODUCTION

The impact of Human Immuno-deficiency Virus (HIV) and Tuberculosis (TB) co-infection is one of the major public health challenges(1). According to the WHO, the risk of developing TB is estimated to be 16-22 times greater in people living with HIV than among those without HIV infection. In 2015, there was an estimated 10.4 million cases of TB disease globally, including 1.2 million (11%) among people living with HIV. Almost 60% TB cases among people living with HIV were not diagnosed or treated resulting in 39,000 TB-related deaths among people living with HIV in 2015(2). In India, about 62% of HIV positive patients are coinfecting with TB making it the most common opportunistic infection(3). CD4 T cell count is critical in control of TB, as qualitative and quantitative decline of the effector cells increases the rate of primary and reactivation of the disease. TB occurs throughout the course of HIV, unlike other opportunistic infections which have a selective range of CD4 counts in which the disease occurs(4). Estimation of CD4 T-lymphocytes is one of the measures of ascertaining the immunocompetence of HIV infected individuals. This test is usually performed in patients on Antiretroviral therapy (ART) to know the response to the treatment(5).

### AIM

Evaluation of CD4 counts in HIV/TB coinfecting patients before and after ATT.

Observe for recovery of CD4 T cell count after ATT.

### MATERIALS AND METHODS

After obtaining approval from the Institutional Ethics Committee, the retrospective study was conducted with the help of the data base available in the Government general hospital, Kakinada. During the period June 2016- August 2017, about 186 patients were found to be coinfecting with HIV/TB. They were included in the study. Details regarding age, sex, duration of HIV, ART, type of TB (pulmonary or extra pulmonary) and ATT were collected. Data of CD4 T-cell counts before and after 6 months of ATT, previous history of TB, contact with TB infected individuals, presence of opportunistic infections and other associated medical conditions were collected.

HIV seropositivity in these patients was diagnosed by using NACO (National AIDS Control Organisation) SD Bioline, Comb AIDS and Tri-spot test kits, the results were interpreted as per manufacturers instruction and diagnosis was done as per national guidelines.(6)

Pulmonary TB was diagnosed when either sputum smear was positive for AFB or by clinical / X-ray finding strongly suggestive of TB or by CBNAAT GeneXpert results.

Extra pulmonary TB was defined as involvement of organs other than lungs like lymph nodes, pleura, meninges, pericardium, abdomen,

bladder, joints and spine. Diagnosis was done when either specimen smear was positive for AFB/CBNAAT GeneXpert results/histopathological proof or radiological evidence or by strong clinical suspicion.

CD4 T- lymphocyte count was performed by a BD FACS COUNT CD4 software version 1.0.

All the data collected was statistically analysed with SPSS software for windows, version 20.0.

### RESULTS

In the study group of 186 HIV/TB coinfecting patients, 160 had pulmonary TB and 26 had extra pulmonary TB.

**Table-1 Distribution of cases of Tuberculosis**

Tuberculosis	Frequency	Percent
PTB	160	86.02
EPTB	26	13.9
TOTAL	186	100

Out of the 160 patients of PTB, 98 were male and 62 were female, among the 26 EPTB cases 16 were male and 10 were female.

Incidence of both PTB and EPTB was found to be highest among the age group of 31-50 years. In the age group of > 50 years, no case of EPTB was observed and among the PTB cases in this age group CD4 counts were found to be low with a minimal recovery after treatment. Table-II shows age-wise distribution of disease along with their CD4 counts.

**Table-II CD4 counts in different age groups**

Age (years)	TB	No. of patients	Mean CD4 before ATT (cells/ $\mu$ l)	Mean CD4 after ATT (cells/ $\mu$ l)
11-30	PTB	58	299	332
	EPTB	12	229	401
31-50	PTB	94	252	327
	EPTB	14	271	394
>50	PTB	8	209	313
	EPTB	0	-	-

Mean CD4 counts prior to antitubercular treatment in pulmonary TB was 266cells/ $\mu$ l (ranging from 15-1113) and in extra-pulmonary TB 248cells/ $\mu$ l (ranging from 13-613). Following treatment, it was 332cells/ $\mu$ l (ranging from 45-1250) in pulmonary TB and 397cells/ $\mu$ l (ranging from 74-1067) in extra-pulmonary TB.

**Table-III Mean CD4 counts before and after ATT**

Treatment status	TB	Mean
Mean CD4 counts after ATT (cells/ $\mu$ l)	PTB	266
	EPTB	248
Mean CD4 counts after ATT (cells/ $\mu$ l)	PTB	332
	EPTB	397

The transition in CD4 counts before and after ATT is statistically significant with p values <0.001 and 0.002 for PTB and EPTB respectively.

## DISCUSSION

TB is the most common opportunistic infection in HIV patients in India (7). In the present study, 86% of study population had PTB, while EPTB was observed in 14%. The magnitude of CD4 T-lymphocytes recovery depends on a variety of factors like maintenance of virologic suppression with ART, age and CD4 count at ART initiation (8).

Bidirectional and synergistic interaction between TB and HIV have additional effect on CD4 counts as compared to HIV alone (9,10). CD4 T-lymphocyte lowering is known to occur in TB patients, who are not affected with HIV (11) and become normal following ATT (12).

In the present study, there was a statistically significant recovery in CD4 counts following ATT and ART. Similar results were reported in other studies by Kavya et al. and Jangid K et al., where there was significant increase in CD4 counts before and after ATT and ART in PTB and EPTB cases with HIV coinfection (5,13).

In a study by Wanchu et al. greater increment in CD4 counts with ATT and ART in dually infected patients was observed (10). There was improvement in CD4 counts following ATT but did not reach statistical significance in a study by Elliott AM, et al. in HIV patients with pleural TB (14). In patients of South Africa with dual infection not receiving ART, mean CD4 count improved from 186 cells/ $\mu$ l at baseline to 239 cells/ $\mu$ l after 6 months of ATT, but this change is not statistically significant (15).

All these studies with significant increase in CD4 count during treatment for TB strongly suggests that TB additionally contributed to subnormal CD4 levels in blood (5,13).

In HIV patients infected with TB, TB adds to the immunological suppression caused by HIV (10). These patients show increased levels of pro-inflammatory cytokines and increased expression of cellular activation markers (17). ATT helps to decrease levels of some of these markers of immune activation and therefore a rise in CD4 cell count is anticipated (18).

## CONCLUSION

There was statistically significant increase in CD4 count after ATT in PTB and EPTB observed in the present study. This increase in CD4 counts with ATT and ART in HIV/TB coinfecting patients suggest that TB additionally influences the reduction of CD4 count in HIV patients.

## REFERENCES

- Ghiya R, Naik E, Casanas B, Izurieta R, Marfatia Y. Clinico-epidemiological profile of HIV/TB coinfecting patients in Vadodra, Gujarat. *Indian J Sex Transm Dis*. 2009;30:10-5.
- World Health Organization. Fact sheet: TB/HIV, 2020. Available at: [https://www.who.int/hiv/topics/tb/about\\_tb/en/](https://www.who.int/hiv/topics/tb/about_tb/en/)
- Sreenivasan Srirangaraj, Dasegowda Venkatesha. Total lymphocyte count as a tool for timing opportunistic infection prophylaxis in resource limited settings: a study from India. *J Infect Dev Ctries*. 2010;4(10):645-9.
- Niraula SR, Barnawal SP, Agrahari AK, Bista N, Yadav DK, Jha N, et al. Prevalence and CD4 cell count pattern of TB co-infection among HIV infected individuals in Nepal. *SAARC J Tuber Lung Dis HIV/AIDS*. 2013;X(1):27-36
- Kavya S, Anuradha K, Venkatesha D. CD4 count evaluation in HIV-TB co infection before and after anti-tubercular treatment. *Int J Res Med Sci* 2014;2:1031-4.
- National AIDS Control Organization. Chapter 6. Guidelines for HIV testing. In: NACO: Ministry of Health and Family Welfare. India: NACO.
- Kumarasamy N, Solomon S, Flanigan TP, Hemalatha R, Thyagarajan SP, Mayer KH; Natural history of human immunodeficiency virus disease in southern India. *Clin Inf Dis*, 2003; 36(1): 79-85.
- Lifson AR, Krantz EM, Eberly LE, Matthew Dolan J, Marconi VC, Weintrob AC; Long-term CD4+ lymphocyte response following HAART initiation in a U.S. Military prospective Cohort. *AIDS Res Ther* 2011, 8(1): 2.
- Swaminathan S, Narendran G. HIV and tuberculosis in India. *J Biosci*. 2008;33:527-37.
- Wanchu A, Kultiatt VS, Sharma A, Singh S, Varma S; CD4 cell count recovery in HIV/TB co-infected patients versus TB uninfected HIV patients. *Indian J Pathol Microbiol* 2010; 53(4): 745-749
- Onwubalili JK, Edwards AJ, Palmer L; T4 lymphopenia in human tuberculosis. *Tubercle*, 1987; 68(3): 195-200.
- Jones BE, Oo MM, Taikwel EK, Qian D, Kumar A, Maslow ER, Barnes PF; CD4 cell counts in human immunodeficiency virus—negative patients with tuberculosis. *Clinical Infectious Diseases*, 1997; 24(5): 988-991

- Jangid K, Shalini M, Shiwangi S, Charoo Hans; CD4 cell count recovery in HIV/TB co-infected patients in a tertiary care hospital. *Sch.Acad.J.Biosci*. 2015;3(6):518-521.
- Elliott AM, Luzze H, Quigley MA, Nakiyingi JS, Kyaligonza S, Namujju PB, Okwera A; A Randomized, Double-Blind, Placebo-Controlled Trial of the Use of Prednisolone as an Adjunct to Treatment in HIV-1—Associated Pleural Tuberculosis. *Journal of Infectious Diseases*, 2004; 190(5): 869-878.
- Morris L, Martin DJ, Bredell H, Nyoka SN, Sacks L, Pendle S, Chaisson RE; Human immunodeficiency virus-1 RNA levels and CD4 lymphocyte counts, during treatment for active tuberculosis, in South African patients. *Journal of Infectious Diseases*, 2003; 187(12): 1967-1971.
- Kalou M, Sassan M, Abouya L, Gelestin B, Chantal M, Mathieu M, et al; Change in HIV RNA viral load, CD4 T cell counts and levels and cotrimoxazole prophylaxis among HIV infected tuberculosis patients in Abidjan. *Journal of Medical Virology*, 2005; 75: 202-208.
- Wallis RS, Vjecha M, Amir-Tahmassebi M; Influence of tuberculosis on human immunodeficiency virus (HIV-1): enhanced cytokine expression and elevated beta 2 microglobulin in HIV-1 associated tuberculosis. *J Infect Dis*, 1993; 167(1): 43-48.
- Lawn SD, Shattock RJ, Acheampong JW, Lal RB, Folks TM, Griffin GE, et al.; Sustained plasma TNF alpha and HIV-1 load despite resolution of other parameters of immune activation during treatment of tuberculosis in Africans. *AIDS*, 1999; 13(16): 2231-2237