

A Study on Patients with TB and HIV Co-Infection in Relation to Mean CD4 Counts

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ABSTRACT

Aim: To study the presentation of HIV-TB co-infection, co-relating the mean CD4 counts with regard to age and gender of the affected individuals. **Methodology:** A cross-sectional study on a total of 334 HIV positive patients diagnosed with tuberculosis was performed and individuals with age more than or equal to 18 years were selected. The data available from patient case records was collected in Performa's. **Results:** In this study, Pulmonary TB was observed in 67.66% and extra pulmonary TB was observed in 32.33% of the individuals with the age group of 18-45 years of age being commonly affected in both Pulmonary and Extra pulmonary TB (85.02%). The mean age at the time of diagnosis was more in pulmonary TB (33.35 years) than in extra pulmonary TB (35.84 years). Males were commonly affected in pulmonary TB (57.96%) whereas females were mostly affected in extra pulmonary TB (56.48%). The mean CD4 counts in pulmonary TB were less (205.66 cells/mm³) than extra pulmonary TB (237.65 cells/mm³) at the time of diagnosis. The mean CD4 counts and age at the time of presentation was less in female (204 cells/mm³, 30.97 years) than males in pulmonary TB which was similar to that in extra pulmonary TB in which females had a mean CD4 count of 201.08 cells/mm³ with 36.50 years as mean age. **Conclusion:** TB still predominates the spectrum of opportunistic infections experienced by the HIV positive individuals manifesting as either pulmonary or extra pulmonary TB. So, special emphasis should be laid in the effective implementation of preventive strategies.

Key words: Pulmonary Tuberculosis, Extrapulmonary Tuberculosis, CD4 counts, Effective diagnosis, Opportunistic infection.

INTRODUCTION

Tuberculosis (TB) in association with Human Immuno Virus (HIV) is a major alarm in the health care system, Mycobacterium tuberculosis in coordination with HIV enhances the descent of immunological functions and pathogenicity of one another leading to death if left untreated¹. The mechanism involved in the progression and the impact of HIV TB co-infection on host's immune system has not been understood completely. The progression has been influenced by factors such as inborn errors of immunity and genetic polymorphisms.¹

Epidemiology

It was estimated that the risk of developing TB was between 26 and 31 times higher in individuals affected with HIV. About 36.7 million people were living with human immunodeficiency virus infection by the end of 2015 (PLHIV) and 2.1 million people became newer targets for HIV. About 1.1 million people died as a result of diseases related to Acquired Immuno Deficiency Virus (AIDS).² Tuberculosis accounts for death in one in every three individuals with Acquired Immuno Deficiency Syndrome (AIDS) related illnesses.³ The incidence of HIV TB co-infection in India was about 2,840 thousands and the mortality due this co-

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infection was about 37 thousands as per the estimation of WHO done in 2015.⁴

Pathophysiology of TB

The pathophysiological processes of TB involve partaking of both innate and cell mediated immunity. The innate immune responses involve active connexion of macrophages and dendritic cells (DC) whereas the cell mediated immunity involves the predominance of T lymphocytes. The prime targets for Tuberculosis are macrophages present in the alveoli.¹ The pathogen within the macrophage will be detected by the toll like receptors (TLR) and nucleotide binding oligomerization domain receptors of innate cells, which initiate local inflammatory response. The inflammatory response is characterized by activation of macrophages and dendritic cells. The activated macrophages release reactive oxygen and nitrogen intermediates and elevate the expression of GTPases.¹ The dendritic cells are involved in the phagocytosis of the pathogen in the tissues of the lung. The DCs will also drift to the lymph nodes triggering T lymphocyte mediated adaptive immunity.¹

The cell mediated immunity mediated by DCs encompass predominance of CD4⁺ T lymphocytes of T helper cell type 1. Other cells such as CD8 T cells and CD1 T cells show optimal immune mediated activities by identification of mycobacterial lipids. The activated T cells then release interferon gamma further activating the macrophages and causing the death of mycobacterium by free radical mediated mechanism or phagolysosome formation.¹

HIV – TB Co-Infection

HIV infection causes a rapid decline of immune responses resulting in multiplication of the mycobacterium within the granuloma leading to reactivation of the infection. It was also theorized that there will be an increased replication of HIV at the sites of mycobacterium infection by multiplying within the activated CD4 + T cells and the macrophages accumulating at the site of granuloma. The death of CD4 + T cells within the granuloma also causes the reactivation of the infection. Thus HIV infected individuals with lower CD4 counts are more susceptible for attaining TB rather than individual with higher CD4 counts.⁵

Prompt evidence suggests that there are decreased levels of CD4 cells and increased viral load in bronchoalveolar lavage as well as in pleural fluid in HIV TB co-infected individuals than in TB infected individuals. Various in vitro studies demonstrate that

the pro-inflammatory cytokines such as TNF alpha, IL 1 β , and IL 6 produced by the phagocytosis of mycobacterium aid in the multiplication of HIV-1. Thus HIV TB co-infection is associated with reduced survivability of macrophages and elevated pro-inflammatory cytokines creates a symbiotic environment for the coexistence of both the pathogens.⁵

Thus estimating the CD4 count status will aid in depiction of the clinical condition in patients with HIV/ AIDS. The CD4 counts also act as an index for the identification, assessment and induction of prophylactic therapies for various opportunistic infections (OIs) in high risk individuals.

AIM OF THE STUDY

The aim of the study is to determine the manifestations of HIV TB co-infection presenting as either pulmonary tuberculosis (PTB) or extra pulmonary tuberculosis (EPTB) and also co-relating the mean CD4 counts with age and gender of the affected individuals.

METHODOLOGY

A cross sectional study was conducted at the antiretroviral therapy (ART) centre of Sri Ram Narayan Ruia Government General Hospital (SVRRGGH), Tirupathi for a period of six months from October, 2015 to April 2016. Among a total of 1074 HIV positive individuals attending the ART centre for regular follow up, 324 individuals were found to be associated with TB as co-infection. Data about patient's age, gender, diagnosis of TB, TB manifestations and CD4 counts at the time of TB diagnosis were collected. All the patient above the age of 18 years diagnosed positive for HIV and TB were included in the study. The patients though diagnosed positive for TB but taking treatment outside the ART centre and patients not willing to participate in the study were excluded from the study.

RESULTS

Among 1074 individuals participated in the study, 334 individuals were associated with HIV TB co-infection. The prevalence of TB was found to be 31.09% with PTB in 226 (67.66%) and EPTB in 108 (32.33%) individuals. The most commonly affected age group was 18 – 45 years of age in both PTB and EPTB. Males (131, 57.96%) were mostly affected in PTB whereas females (61, 56.48%) were commonly

affected in EPTB. The age and gender wise distributions were depicted in the Tables 1 and 2.

At the time of diagnosis, the mean CD4 counts in PTB and EPTB were 205.66 cells/mm³ and 237.65 cells/mm³. About 82 (36.28%) PTB affected individuals had a CD4 counts <200 cells/mm³ followed by 70 (30.97%) individuals with CD4 counts ranging between 200 – 500 cells/mm³. In individuals affected with EPTB, about 39 (36.11%) individuals had a CD4 counts ranging between 200 – 500 cells/mm³ followed by the CD4 counts of <200 cells/mm³ in 36 (33.33%) individuals. The no. of individuals who presented with CD4 counts <50 were 27 in PTB and 9 in EPTB respectively. The CD4 count ranges were mentioned in the Table 3 given below.

The mean CD4 counts in males and females were 204.72 cells and 206.34 cells/mm³ with mean ages of 30.97 years and 36.50 years in females and males

Table 1: Age wise distribution of the patients

Age group (years)	Total No. of patients (n = 334)			
	PTB (n = 226)	Percentage (%)	EPTB (n = 108)	Percentage (%)
18 - 45	187	82.74	97	89.81
45 - 65	37	16.37	11	10.18
>65	2	0.88	0	0
Mean age (years)	38.35		35.84	

Table 2: Gender wise distribution of the patients.

Type of TB	Gender			
	Males	Percentage (%)	Females	Percentage (%)
PTB (n = 226)	131	57.96	95	42.35
EPTB (n = 108)	47	43.51	61	56.48

Table 3: CD4 count ranges in PTB and EPTB.

CD4 count ranges (cell/mm ³)	No. of individuals			
	PTB (n = 226)	Percentage (%)	EPTB (n = 108)	Percentage (%)
< 50	27	11.94	9	8.33
< 200	82	36.28	36	33.33
200 – 500	70	30.97	39	36.11
501 – 1200	18	7.96	13	12.03
Unavailable	29	12.83	11	10.18

Table 4: Mean CD4 counts and mean age at the time of presentation.

Gender	PTB		EPTB	
	Mean CD4 counts (Cells/mm ³)	Mean age (years)	Mean CD4 counts (Cells/mm ³)	Mean age (years)
Females	204.72	34.97	201.08	36.08
Males	206.34	36.50	265.83	39.61

respectively in PTB. Where as in EPTB the mean CD4 counts were 201.08 and 265.83 cell/mm³ with a mean age of 36.50 and 39.61 years in females and males respectively. The Table 4 given below shows the differences in mean CD4 counts and age of presentation in both the genders of the affected population.

DISCUSSION

In the present study, the prevalence of TB was found to be 31.09% which was not analogous to the findings of Alfred Muremo *et al.*, who reported a higher prevalence. A similar prevalence of TB as in our observation was reported by Surendra KS *et al.* This change in prevalence can be attributed to the screening of TB and also various other factors such as gender, educational status, residence, occupational status, marital status, CD4 count level and WHO clinical staging.^{6,7}

It was observed that PTB constituted 67.66% and EPTB constituted 32.33% of the study population which was comparable to the findings of Ketki Jangid *et al.*, Nara *et al.*, and Alfred Muremo *et al.*⁶⁻⁸ Our findings were in contrast to those of Harapriya Kar *et al.*, and Kavaya S *et al.*,^{10,11} Usually the incidence of EPTB was more in AIDS as related immunodeficiency inclines to manifest as atypical TB and is also associated with dissemination outside the lung when compared to individuals without HIV.¹²

The mean age of presentation was equivalent to the findings made by Aghor Ako *et al.*¹² The age of presentation of EPTB was less when compared to PTB in our study though there is no demarcated difference. The most commonly affected age group was 18 – 45 years in both PTB and EPTB which was similar to the outcomes seen by Nara *et al.* and Siddeshwari *et al.*⁹⁻¹³ Usually age > 35 years, cough > 2 weeks duration, night sweats, severe wasting, presence of pleural effusion, positive HIV status and anemia were considered as the predictors of TB.⁶

In concern to the gender wise distribution majority of the males were affected with PTB and females were affected with EPTB which was in co-relation with the observations of Aghor AKO *et al.*¹² and the mean age was less in females when compared to males for both PTB and EPTB. Usually women were found to have higher susceptibility to HIV infection and were exposed to sexual activity earlier than men and also being HIV positive for 10 years was considered to be a risk factor for presentation of EPTB⁹⁻¹² So, this contributes to the practical inference that women were presenting at younger ages than men and were more susceptible to EPTB than men.

The mean CD4 counts in EPTB were more to that in PTB and the mean counts were comparable with the findings of Ketki Jangid *et al.*⁸ But the mean CD4 counts for EPTB were lesser than PTB which was not in accordance with our findings. The decline in the CD4 counts at the time of diagnosis can be considered as the indication for the presence of OI and also as a marker for the symbiotic association between TB and HIV. The studies performed by Kavya S *et al*, Nara *et al.*⁹⁻¹¹ stated that EPTB was most commonly observed when the CD4 counts were <200 cells/mm³. Also EPTB presenting as meningitis and CD4 T cells <200 cells/mm³ were considered as the increased risk factors for mortality⁶. But, in our study the mean CD4 counts for EPTB were 237.65 cells/mm³ which should be considered as a determining factor for diagnosis and needs to be correlated with the clinical findings.

CONCLUSION

In HIV positive individuals TB still remains to be the commonly observed opportunistic infection presenting even at higher CD4 counts. The health care professionals should consider differential diagnosis for TB as most of the individuals present with smear negativity. Employing culture sensitivity tests and gene expert tests in individuals with potential risk factors should be considered. There is a need to implement prophylactic therapies in high risk individuals by considering symptomology and clinical staging. Individuals receiving prophylactic regimens had a lower risk of mortality. There is also a prompt necessity to conduct mass screening programmes to detect newer cases of TB in HIV infected individuals.

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CONFLICT OF INTEREST

None

ABBREVIATION USED

TB: Tuberculosis; HIV: Human Immunodeficiency Virus Infection; PLHIV: People Living with Human Immunodeficiency Virus Infection; AIDS: Acquired Immunodeficiency Syndrome; CD4: Cluster of Differentiation; DCs: Dendritic Cells; TLRs: Toll Like Receptors; GTP: Guanosine Tri Phosphate; TNF: Tumour Necrosis Factor; IL: Interleukins; OIs: Opportunistic Infections; PTB: Pulmonary Tuberculosis; EPTB: Extrapulmonary Tuberculosis; ART: Anti Retroviral Therapy.

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