



*Original article*

## Treatment Outcome of Tuberculosis in Seropositive Patients in a Tertiary Care Hospital and ART Centre in Mumbai, India

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### ABSTRACT

**Background:** Tuberculosis is one of the major health problems in India. The Tuberculosis problem is further aggravated by TB- HIV co-infection. TB is not only leading cause of death in HIV infected persons but it also accelerates the progression of HIV infection to AIDS, at the same time, HIV infection is amongst the strongest risk factor for progression of latent TB infection to active disease. However the principles of TB control are the same, treatment with DOTS (Directly Observed Treatment, Short course) is the accepted standard even for HIV positive TB patients. **Methods:** The present study was conducted to assess the treatment outcome of TB in TB-HIV co-infected patients on DOTS. A Prospective observational study was conducted at ART [Anti Retroviral Therapy] centre of B Y L Nair Charitable hospital, Mumbai, India. The newly diagnosed TB patients receiving DOTS were registered and were followed till treatment outcome was declared. **Results:** The treatment success rate was found to be 89.32% (92 of 103 patients). Higher treatment success rate was seen among patients with CD<sub>4</sub> count >200/  $\mu\text{L}^3$  at the time of diagnosis, WHO clinical stage 1 and 2, and among working patients than ambulatory. No significant association was found with concurrent Anti Retro Viral Therapy and socio economic classes. **Conclusion:** The DOTS was found to be as effective in HIV seropositive, so it should be strengthened, in order to control the HIV-TB epidemic.

**KEYWORDS:** CD<sub>4</sub> count, DOTS therapy, TB-HIV co-infection, WHO staging of HIV infection

### INTRODUCTION

Tuberculosis is one of the major health problems in India, with India accounting for 20% (2 million of 9.4 million incidence cases of TB in year 2009) of world's tuberculosis cases [1]. The Tuberculosis problem is further aggravated by TB- HIV co-infection. India, the third highest HIV burden country, had an estimated 2.39 million (translating to a prevalence of 0.31%) PLHA [People Living with HIV/AIDS]. It has been

estimated that in 2009, about 6.4% (3.9-9.8%) of the incident TB cases in India were HIV-positive [2]. TB is not only leading cause of death in HIV infected persons but it also accelerates the progression of HIV infection to AIDS. HIV infection is amongst the strongest risk factor for progression of latent TB infection to active disease.

The principles of TB control are the same even when there are many HIV/TB patients. Treatment with DOTS (Directly Observed Treatment, Short course) is the accepted standard even for HIV positive TB patients [3, 4]. With the emergence of HIV epidemic, health services struggle to cope with the large and rising number of TB patients with consequences like low treatment success rate and high mortality. The present study was conducted to assess the treatment outcome of TB in TB-HIV co-infected patients on DOTS, attending Drop In Centre and ART centre attached to a tertiary care hospital in Mumbai, India.

**Aim:** To study the treatment outcome of tuberculosis among TB-HIV coinfecting patients, attending Drop in Centre/ART centre at a tertiary care hospital of South Mumbai, India.

**Objectives:** 1).To study the clinical profile of TB patients co-infected with HIV 2). To follow up the Study group till treatment outcome is declared. 3).To highlight the factors influencing treatment outcome.

## MATERIALS AND METHODS

*Study design:* This Prospective observational study was conducted at the Drop In Centre and ART centre of B Y L Nair Charitable hospital, Mumbai, India. This ART centre, attached with tertiary care hospital provides services to vast area of Mumbai, specially south and central region. The Drop In Centre provides preventive services to people diagnosed with HIV infection, i.e. distribution of condoms, nutritional supplements along with counselling, yoga therapy, group therapy and support to family members.

*Study Period:* January 2010 to Dec 2011.

*Study Population:* A total 103 seropositive patient registered at the ART centre of B Y L Nair Charitable hospital, Mumbai, who were diagnosed with Tuberculosis and started on the DOTS during the period of 1<sup>st</sup> January to 30<sup>th</sup> June 2010 were included in the study. These patients were followed up for a period of one year or till treatment outcome was declared. Since the ART centre provides service to a vast area of Mumbai, only patients residing in South Mumbai (Municipal Corporation Wards A to E) were included in the study, making it feasible to follow up in case of treatment default.

### *Exclusion Criteria:*

1. Seriously ill patients requiring in-patient treatment.
2. Patients on Non-DOTS regimen for Tuberculosis.

The patients were interviewed at OPD with pre-tested semi structured interview schedule. Necessary data regarding demographic profile, Socio-Economic Status, past and present tuberculosis history including treatment and adverse drug reactions was collected. In TB-HIV co-infected patients, information about Basic CD4 count at the time of TB diagnosis, WHO Clinical and Functional staging [5] and Anti Retroviral Therapy was also collected. These patients were followed up every month for next 6 to 9 months, till the treatment outcome was declared. It was not possible to follow up all the patients by home visits, as stigma related to tuberculosis is still there in the community.

On each visit patient's health status was assessed by clinical examination (Deterioration of condition, if any and weight gain) and sputum AFB reports done at DOTS centre. The each opportunity of interaction with patient or his relatives was capitalized for educating them, regarding importance of treatment completion, proper nutrition, proper disposal of sputum, regular health check-ups, and DOTS therapy. Patients were advised to visit the nearest hospital or DOTS centre, in case any adverse reaction from the drugs occurs.

At least 3 Follow ups were done during the period, preferably at time of scheduled sputum examination. Basic parameters used for follow up were: clinical improvement, weight gain, sputum conversion. Ethical Clearance was obtained from institutional ethical committee.

*Statistical Analysis:* The data was thoroughly analysed using S.P.S.S. 16. Descriptive statistics: Frequency distribution and percentage. Test of significance is Chi square test.

## RESULTS

In this study maximum (62.13%) patients were in 21-40 years age group with mean age 37.2 years (Std Deviation: 10.3 Years, Range: 17-65 Years).

Maximum TB-HIV infected patients were male (Male to female ratio-3:1), married (64.1%), and belonged to Low Socioeconomic Class (Kuppuswamy Scale- Lower and upper lower classes-77.67%) (Table-1).

**Table 1: Demographic Profile of TB-HIV coinfecting patients (n=103)**

	Group	Seropositive Cases (No & percent)
Age Group	up to 20 years	5 (4.9)
	21-30 Years	19 (18.4)
	31-40 Years	45 (43.7)
	41-50 Years	23 (22.3)
	51-60 Years	9 (8.7)
	>60 Years	2 (1.9)
Sex Distribution	Male	76 (73.8)
	Female	27 (26.2)
Marital Status	Unmarried	25 (24.3)
	Married	66 (64.1)
	Separated/Divorced	2 (1.9)
	Widow/Widower	10 (9.7)
Education Status	Illiterate	26 (25.2)
	Up to Primary	35 (34.0)
	Secondary	27 (26.2)
	Higher sec	8 (7.8)
	Grad & above	7 (6.8)
Occupation	Unemployed	39 (37.86)
	Unskilled	19 (18.45)
	Skilled	41 (39.80)
	Professional	4 (3.88)
Socio-Economic Class	Lower	30 (29.13)
	Upper Lower	50 (48.54)
	Lower Middle	14 (13.59)
	Upper Middle	9 (8.74)

The common symptoms of tuberculosis disease were Fever (80.6%), Cough (65%) and weight loss (55.3%). By eliciting H/o Fever and cough for a duration of >2 weeks, 2/3<sup>rd</sup> of tuberculosis suspects can be identified. While triad of Fever, cough and weight loss was present in 35% cases (Table-2).

On general examination, presence of pallor was most common finding (56.31%), followed by lymphadenopathy (18.45%). On systemic examination, abnormal respiratory findings were present only in 1/4<sup>th</sup> of patients. 17.48 % had abnormal per abdomen findings in form of tenderness (Table-3).

**Table 2: Clinical profile of TB-HIV coinfecting patients (n=103)**

Symptoms	Seropositive Cases ( No & percent)
Fever	83 (80.60)
Cough	67 (65)
Weight Loss	57 (55.34)
Abdominal pain	39 (37.90)
Lymphadenopathy	19 (18.45)
Haemoptysis	6 (5.83)
Triad of Cough > 2 weeks , fever and weight loss	37 (35.9)
Cough > 2 weeks and Fever	64 (62.1)

**Table 3: Examination Finding of TB-HIV coinfecting patients (n=103)**

Examination Finding	Seropositive Cases ( No & percent)
Pallor	58 (56.31)
Lymphadenopathy	19 (18.45)
Abnormal respiratory finding	27 (26.21)
Abnormal P/A finding	18 (17.48)

Out of 103 TB –HIV coinfecting patients, 40 (38.83%) had past history of Tuberculosis (Category two) and 63 (61.17%) were new cases. Among TB-HIV coinfecting patients, extrapulmonary tuberculosis (EPTB) was the predominant type of Tuberculosis (55.34%), the commonest site being peripheral Lymph nodes (25 out of 57 cases,43.85%) followed by Abdominal tuberculosis (23 out of 57, 40.35%) and Pleural effusion (15.79%). Pre treatment sputum smear microscopy was positive in only 1/4<sup>th</sup> cases (Table-4).

Out of 103 patients, 60 cases (58.25 %) were on ART. Majority of cases belonged to WHO clinical stage 3 (26.21%) and stage 4 (34.95%), and Functional Staging-Working (66.69%). Bedridden cases were not included in the study. Nearly half of the patient had CD<sub>4</sub> count below 200/  $\mu\text{L}^3$  at the time of Tuberculosis diagnosis (Mean CD<sub>4</sub> count= 218 cells/  $\mu\text{L}^3$ , CD<sub>4</sub> count Range= 15-725 cells/  $\mu\text{L}^3$ ) (Table-5).

During treatment course, the commonest adverse reactions experienced by patients were Nausea (52.43%) and Vomiting (50.48%). A few patients experienced Rashes (8.74%), Joint pain (6.8%), Jaundice (6.8%), hyper pigmentation (1.94%) and Apathous ulcers (1.94%).

*Follow Up:* During treatment course, Intensive Phase was extended by a period of one month in 6 cases (5.83%), treatment discontinuation due to adverse drug reactions was seen in 7 cases (6.8%). The reasons for discontinuation of treatment were development of jaundice and hypersensitivity reaction to streptomycin. Mean weight gain during the follow up period was 4.14 kg (Range: 0-11 kg).

*Treatment Outcome:* In the study group 92 (89.32%) patients had the desired treatment outcome (Either cured or treatment completed). Of the remaining 11 patients 3 (2.91%) were treatment failure and 6 (5.88%) were transferred

out and 2 (1.94%) died during the treatment. Treatment success rate of Tuberculosis among seropositive patients was significantly associated with CD<sub>4</sub> Count, WHO clinical and Functional staging. Higher treatment success rate was seen among patients with CD<sub>4</sub> count >200/  $\mu\text{L}^3$  at the

time of diagnosis, WHO clinical stage 1 and 2, and among working patients than ambulatory. No significant association was found with concurrent Anti Retro Viral Therapy and socio economic classes (Table-6).

**Table 4: Present disease characteristics of the group (n=103)**

Disease Characteristics		Frequency (Percentage)
Type of disease	Pulmonary	46 (44.66)
	Extra pulmonary	57 (55.34)
Treatment Category	One	63 (61.17)
	Two	40 (38.83)
Pre treatment Sputum smear examination finding	Positive	26 (25.24)
	Negative	77 (74.76)
Type of case	New	63 (61.16)
	Relapse	13 (12.32)
	TAD	14 (13.6)
	Other	13 (12.62)
	Failure	0 (0)

**Table 5: Basic Information about ART, CD4 count, and staging of the study group (n=103)**

Variable		Frequency (Percentage)
Anti Retroviral Therapy	Yes	60 (58.25)
	No	43 (41.75)
WHO Clinical Staging	Stage 1	30 (29.13)
	Stage 2	10 (9.71)
	Stage 3	27 (26.21)
	Stage 4	36 (34.95)
Functional Staging	Working	69 (66.99)
	Ambulatory	34 (33.01)
	Bedridden	0 (0)
CD4 count at the Start of AKT (in $\mu\text{L}^3$ )	<200	49 (47.57)
	200- <350	32 (31.7)
	>350	22 (21.36)

**Table 6: Factors predicting treatment outcome of Tuberculosis in seropositive patients (n=103)**

Factors		Cured & Completed (n=92)	Other* (n=11)	Total	$X^2, df, P$
ART	Yes	52 (86.67)	8 (13.33)	60	0.499, 1, 0.48
	No	40 (93.02)	3 (6.98)	43	
Socio Economic classes	Upper Middle	8 (0.88)	1 (0.12)	9	0.001, 1, 0.972
	Lower middle	13 (92.86)	1 (7.14)	14	
	Upper lower	44 (88)	6 (12)	50	
	Lower	27 (90)	3 (10)	30	
CD <sub>4</sub> Count (/ $\mu\text{L}^3$ )	<200	40 (81.63)	9 (18.37)	49	6.325, 2, 0.04
	200-<350	30 (93.75)	2 (6.25)	32	
	>350	22 (100)	0 (0)	22	
WHO Clinical staging	1	31 (100)	0 (0)	31	4.002, 1, 0.04
	2	11 (91.67)	1 (8.33)	12	
	3	21 (84)	4 (16)	25	
	4	29 (82.86)	6 (17.14)	35	
Functional staging	Working	66 (95.6)	3 (4.4)	69	5.052, 1, 0.02
	Ambulatory	28 (82.3)	6 (17.7)	34	

\* Includes treatment outcome other than cured and completed.

## DISCUSSION

In present study tuberculosis mainly affected the age group 21-40 years, with male predominance (Male to female ratio- 3; 1). This finding is in accord with finding of Tripathy S et al, 2011[6] and Vijay S et al 2011[7]. Majority of TB-HIV coinfecting patients belonged to low socioeconomic status, this is in accordance to a study done in South India on risk factors for TB by Shetty et al 2006[8], which showed that Tuberculosis most commonly affects lower socioeconomic class population (Low income and low education).

In our study, the common presenting features of tuberculosis disease were Fever (80.6%), Cough (65%) and weight loss (55.3%). In a study conducted by Ahemad Z et al 2005 [9] on "Manifestation of Tuberculosis in HIV infected patients", fever was found to be the commonest

presenting symptom (89%) followed by anorexia (84%), cough (83%), profound weight loss (79%), and weakness (77%). In the series reported by Mohanty et al [10], Gupta et al [11] and Purohit et al[12] fever was the most common complaint. In our study, the most common type of Tuberculosis affecting the HIV infected patients was extrapulmonary, affecting the 57 out 103 (55.34%) patients. Studies done in past had shown 30 to 50% prevalence of extra pulmonary TB among HIV infected individuals. Kumar P et al 2002 [13], Ahemad Z et al 2005[9] and Gupta P et al 2006[14] found prevalence of EPTB in HIV infected patients 45.3%, 38.46% and 35.71% respectively.

Recent studies have shown increased involvement of Extra Pulmonary sites in TB-HIV coinfecting individuals in more than half cases. Patel et al 2011[15] reported 60 % extra pulmonary

tubercular involvement while Sophia Vijay et al 2011[7] reported that 50% cases were suffering from extrapulmonary tuberculosis, and the commonest form of EPTB was lymph node involvement (34%) followed by pleural effusion (28%).

Positive sputum smear results were seen only in 1/4<sup>th</sup> patients. Various studies done by Kumar P et al 2002 [4], Ahemad Z et al 2005[9], Gupta P et al 2006[14] Rajasekaran et al 2007[16] and Patel, et al 2011[15] have shown positive sputum smear results in 20-40% TB-HIV coinfecting patients. The most common site of EPTB was peripheral lymph nodes followed by abdominal lymph nodes and pleural effusion. In the study group most commonly involved lymph nodes were cervical (40.35%) followed by abdominal nodes (38.59%). Axillary nodes were involved in 3.51% cases.

During the treatment course 70.8% (73 out of 103) patients experienced one or another adverse reaction while on AKT (Anti Koch's Treatment). The prevalence of adverse reaction in patients with concurrent ART was 86.67% (52 of 60 patients), while in patients taking only AKT was 48.83% (21 of 43 patients). This difference was statistically significant with chi square value 15.581 and p Value < 0.001. This significant difference could be because of overlapping spectrum of adverse reaction of ART and AKT.

In present study treatment success rate (treatment completed and cured) was 89.3%. 3 cases were declared as treatment failure (2.91%), while there was no defaulter during the treatment. Failure rate of 2.91% was less than the RNTCP norm of <4% of patients put under DOTS. 2 patients died during the treatment, death rate of 1.94% is just as par with RNTCP norm of < 2% death rate. Treatment outcome was higher in our study when compared to other studies done by Vijay S et al 2011[7], Chennaveerappa PK et al [17] and Tripathy S et al 2011[6], which showed 66-83% treatment success rate.

The high treatment success rate and low mortality rates in our study can be explained by the fact that

seriously ill patients were excluded from the study and possible role of ART in improved tuberculosis treatment outcome, though in our study we did not find any significant association between TB treatment outcome and Anti Retroviral Therapy.

## **FACTORS AFFECTING TREATMENT OUTCOME**

TB is a disease of poverty and commonly affects the lower socio economic classes but its treatment outcome does not differ significantly amongst various socio economic classes. This may be because of freely availability of DOTS therapy.

The treatment outcome of HIV seropositive TB was significantly associated with CD<sub>4</sub> counts, which was reflected by advanced clinical stage and poorer functional stage (ambulatory and bedridden). The association of CD<sub>4</sub> count and treatment outcome was also shown in various studies. Chideya S et al 2009 [18] reported that HIV-infected patients with a CD<sub>4</sub> cell count <200 cells/ $\mu\text{L}^3$  had a higher risk of poor treatment outcome (27%) than did HIV-uninfected patients (11%) or HIV-infected patients with a CD<sub>4</sub> cell count > 200 cells/ $\mu\text{L}^3$  (P=0.01). In a prospective, randomized controlled trial, Chamie G et al 2010 [19], found that triple nucleoside ART does not accelerate microbiologic, clinical or radiographic improvement during TB therapy in HIV/TB patients with high CD<sub>4</sub> counts (CD<sub>4</sub> counts> 350).

## **RECOMMENDATION**

In view of increasing prevalence of extrapulmonary tuberculosis in HIV patients as well as in general population, the health professionals should be trained in diagnosing and if necessary referral.

The DOTS is found to be as effective in HIV seropositive, so it should be strengthened, in order to control the HIV-TB epidemic.

*Limitation of the study:* In order to generalize the findings, similar type of study should be done on a wide scale involving seriously ill TB patients along with patients taking treatment on OPD basis.

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