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Treatment Outcome Analysis of Drug-Sensitive Pulmonary and Extrapulmonary Tuberculosis Among HIV Positive and HIV Negative Patients and their Correlation with CD4 Counts

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Abstract

Background: WHO guidelines recommended daily therapy in HIV-TB co-infected individuals. The study was aimed at comparing treatment outcomes of standard drug-sensitive anti-tuberculosis regimen in HIV seropositive and HIV seronegative patients with tuberculosis and their correlation with CD4 counts.

Material & methods: The present observational and prospective study of 236 HIV-negative and 154 HIV-positive patients was conducted over two years. All the patients included in the study were reviewed regularly to enquire the compliance, symptom improvement and outcome analysis.

Results: Among HIV-negative patients, pulmonary TB was more common, while among HIV-positive patients, extrapulmonary TB was observed more frequently. Notably high treatment success rate (82.6 vs. 65.5% at the end of treatment, p-value 0.002) and low mortality rate (8.0 vs. 20.1%, p-value 0.002) were observed among HIV-negative patients. Higher CD4 counts among HIV-positive patients was found to be noteworthy after 6 months treatment (194.85 vs. 288.18, p <0.001). Those HIV individuals who died had inadequate improvement in CD4 counts.

Conclusions: Overall, HIV negative patients did better on the daily DOTS regimen than HIV positive patients in terms of treatment completion and success rates, treatment failure as well and mortality. Improvement in CD4 counts after treatment was statistically significant and indicates the effectiveness of combined ART and DOTS in tuberculosis treatment.

Keywords: Tuberculosis, HIV infection, Treatment outcome.

Introduction

Tuberculosis (TB) continued to have a significant impact on morbidity and mortality despite having highly effective treatment. India accounts for 28 lakh annual incidence and mortality of 4.8 lakhs, which accounts highest number of TB and MDR TB cases in the country as per the global TB report published by the WHO.[1,2]

The National Tuberculosis Program was started in India in 1962 and was revised in 1997 as the "Revised National Tuberculosis Control Programme" (RNTCP) that used WHO WHO-recommendednded (directly observed treatment short course [DOTS] chemotherapy strategy. Although DOTS was implemented across the nation by 2006, the TB cases continued to rise, simultaneously with increasing relapses and drug-resistant TB cases.[3]

Since March 2016, RNTCP observed a major change and instituted a daily DOTS regimen with "fixed dose combination" (FDC) for the treatment of TB in an effort to make the treatment more effective, to decrease the relapses and the incidence of drug resistance.[4] This strategy for daily

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DOTS was first implemented at ART centres as 99DOTS, which was an immediate and budget-friendly solution for observing and enhancing medication adherence.

Human immunodeficiency virus (HIV) and Tuberculosis (TB) are the most important contributors to morbidity and mortality worldwide[5,6]. Even with significant progress in TB control recently[7], the HIV epidemic has posed a major challenge as HIV and TB co-infection[7-9]. There is much discussion over how anti-tuberculosis therapy (ATT) should be given to HIV patients, given their immune-compromised state, possible drug-drug interactions[10,11], higher mortality rate[5-8,12-14] and variable presentation and organ involvement[7,10,11].

There is are paucity of studies comparing the efficacy of daily DOTS regimens among HIV positive and HIV negative patients. So that, a study was taken up to compare the efficacy of a daily anti-tuberculosis regimen in HIV seropositive and HIV seronegative patients having tuberculosis and their outcome correlation with CD4 counts

Material & Methods

Source of data

The study was conducted in patients admitted to or attending the outpatient department of Respiratory Medicine and the ART Centre of our institution.

Inclusion criteria

- All new cases diagnosed with drug-sensitive TB, both Pulmonary and extrapulmonary TB, taking or willing to take daily DOTS.
- Compliant HIV positive individuals on ART and daily DOTS.
- Age >18 years.

Exclusion criteria

- Patient refused DOTS and or ART
- Pregnant females
- Co-morbid illnesses such as poorly controlled diabetes mellitus, cardiac failure, renal dysfunction, occupational lung disease, coexisting lung cancer or bronchiectasis and any other malignancy on chemotherapy, etc., at initial presentation
- Patients with other opportunistic infections
- Patients who needed modified regimens because of significant adverse drug reactions

Duration of study

Over a period of one year

Study design and case selection

This was a prospective observational study where all social classes were represented, but the majority were in lower groups. Patients aged between 18 to 65 years with active TB (new cases or having a history of less than one month of anti-tuberculosis treatment) were consecutively assessed for enrolment. These patients were then divided into two groups: one group with a new or existing HIV infection, and HIV-negative patients in the other group. Approval was obtained from the institutional ethical committee. Written and informed consent was also obtained from all patients.

The socioeconomic and demographic data of the study cases were obtained from the treatment cards and structured interviews. A detailed clinical history, along with previous history of ATT, including type and site of TB, diagnostic methods and sensitivity results, was also recorded. The modified Kuppuswamy socioeconomic scale was used to classify socioeconomic status.

Information about the co-morbidities, including HIV status, diabetes and others, stated as above in exclusion criteria, was also obtained as a part of the history and necessary investigation.

Diagnosis and baseline assessment

All study subjects were consulted and tested for HIV by using an ELISA kit[15] at the ICTC centre of the institute. TB was diagnosed on the basis of investigations as indicated, depending on the site of involvement, such as smear microscopy, CBNAAT & mycobacterial culture of sputum or body fluids, secretions, tissue, or pus (wherever necessary); cytology/histology and cytopathological examination of tissues or fluid (including broncho-alveolar lavage if required); and several imaging modalities. For example, all subjects with suspected smear-negative pulmonary TB patients underwent broncho-alveolar lavage smear and CBNAAT, whereas on fluids from extrapulmonary sites such as cerebrospinal fluid, pus from cold abscess and pleural aspirates, CBNAAT was regularly performed.

TB was classified as microbiologically confirmed based on diagnosed by smear, culture, or CBNAAT/LPA or clinically diagnosed based on suggestive radiology, histology, cytology, or fluid biochemistry[16]. All patients underwent baseline clinical evaluation, chest x-ray and blood routine tests (complete blood counts, blood sugar, renal and liver function tests, electrolytes etc). HIV positivity was diagnosed by using NACO (National AIDS Control Organisation) supplied test kits such as Comb AIDS, Tridot and Triline and interpreted as per the manufacturer's instructions and diagnosis was made as per national guidelines[17]. CD4 count was performed with a FACS (Fluorescent Assisted Cell Sorter) counter, with labelled antibodies. CBNAAT of samples was performed using MTBDR plus, version 2.0, Hain Life Sciences, Nehren, Germany. In pulmonary TB, chest radiographs were also ordered. A diagnosis of TB pleural effusion was made based on fluid biochemistry, fluid CBNAAT, or pleural biopsy. A diagnosis of tubercular lymphadenitis was made on the basis of either FNAC suggestive of caseating granulomas, AFB positivity, or CBNAAT of pus aspirated. Abdomen TB diagnosis was made based on a suggestive clinical picture, ultrasound/CT Abdomen, ascitic fluid analysis, CBNAAT, along with the opinion of a gastroenterologist. Spinal TB was diagnosed based on typical MRI findings with or without a

psoas abscess. A diagnosis of TB Meningitis was based on typical CSF findings, MRI brain and CSF CBNAAT.

Treatment

All patients received standard daily DOTS therapy according to the National TB Elimination Programme guidelines. This consisted of isoniazid, rifampicin, pyrazinamide and ethambutol for 8 weeks in the intensive phase as per weight band categories, followed by isoniazid, rifampicin and ethambutol 16 weeks in the continuation phase, as a fixed dose combination.

All HIV-positive patients received highly active ART as per National AIDS Control Organisation guidelines. All HIV infected patients also received prophylactic co-trimoxazole therapy as per guidelines[18].

Follow-up

Follow-up visits were conducted biweekly during the initial two months of the treatment, then monthly up to the end of treatment. Follow-up using a structured format, included clinical evaluation, assessment for opportunistic infections (in HIV-seropositive patients), routine blood investigations, including haemoglobin, renal and liver functions, to monitor adverse reactions to treatment. In pulmonary TB patients, sputum smear was performed as per protocol, every two months. Chest radiographs were also done as and when required. CD4 cell counts were measured at the time of starting treatment and 6 months after starting treatment in all HIV positive patients.

Adherence was ensured at each visit to the DOTS or ART centre (monthly) through direct questioning and the use of blister packs. This was further supported by medical social workers or TB health visitors. Adverse events, if any, were also communicated to the ethical committee.

Statistical analysis

All participants who received at least one month of ATT were included in the treatment outcome analysis. Comparisons between both groups were analysed by using Fisher's exact or Pearson chi-squared tests for categorical data, and unpaired t-test or Wilcoxon Rank-sum test for the qualitative characteristics. A *p-value* <0.05 was considered statistically significant. All analyses were carried out using Epi Info version 7.2.1.0 statistical software. Outcome operational definitions were defined as per guidelines.[19]

Results

This study included 396 subjects after applying the inclusion and exclusion criteria. The mean age was 35.83 ± 10.84 years in HIV positive and 38.48 ± 11.19 years in HIV negative. The majority of them were male in both the groups (74% HIV Positive and 68.3% HIV Negative).

Most HIV positive TB patients belonged to lower (46.8%) or upper lower socioeconomic status (39%), whereas most HIV negative TB patients belonged to lower middle (35.6%) and upper lower socioeconomic status (28.8%) according to the modified Kuppuswamy Scale.

The mean weight of HIV positive cases (43.92 kg) and HIV negative cases (44.62 Kg) was not significantly different (p = 0.508). The mean weight increased significantly in HIV positive patients (from 23.92 to 49.41 Kg) at 6 months follow-up (p <0.001). Among HIV negative patients, the mean weight also increased from 44.62 to 46.46 Kg, but this was not statistically significant (p = 0.051) (Table 1).

Among HIV negative patients, Pulmonary TB was more common (87.2%), while among HIV positive patients extra pulmonary TB was more common (59.1%) as compared to pulmonary TB (40.9%). This difference in type of TB among HIV positive and negative patients was found to be statistically significant (p <0.001) (Figure 1).

Abdominal TB was the most prevalent form of extrapulmonary TB in individuals with HIV positive status (53.8%), while among HIV negative patients, pleural effusion (46.6%) was the most common form, followed by abdominal TB (33.3%). This difference was not statistically significant. (p>0.05) (Table 2). The incidence of TB lymphadenopathy and bony tuberculosis was similar in the two groups.

Table 1: Demographic profile of study participants

	HIV positive	*HIV negative*
Age (MEAN ± SD)	35.83 ± 10.84	38.48 ± 11.19
Gender (M:F)	114 : 40 (2.85:1)	164 : 76 (2.16:1)
Weight in KG at baseline (Mean ± SD)	43.92 ± 10.14	44.62 ± 10.38
Weight in KG at 6 months (Mean ± SD)	49.41 ± 9.87	46.46 ± 9.37
Socioeconomic status		
Lower class	72 (46.8%)	64 (27.1%)
Upper lower class	60 (39.0%)	68 (28.8%)
Lower middle class	15 (9.7%)	84 (35.6%)
Upper middle and upper class	7 (4.5%)	20 (8.4%)

Figure 1: Shows the distribution of pulmonary and extrapulmonary TB among the study participants.

Outcome analysis

The Treatment success rate was significantly higher in non-HIV patients (82.6%), in contrast to HIV positive patients (65.5%) and this difference was statistically significant (p <0.001) (Refer to Table 5 for breakup of treatment success group of patients). The death rate (20.1 vs 8.0%) and lost to follow-up (13.0 vs 7.2%) were higher in the HIV-positive than the HIV-negative patient group. This difference in outcome among HIV positive and HIV-negative patients was statistically significant (p = 0.002) (Table 3).

(*Treatment success = Cured + Treatment completed)

At baseline, among HIV positive patients with pulmonary TB, 39.7% were sputum smear positive, while among HIV negative patients, only 20.8% were sputum smear positive and this difference was considered to be statistically significant (p-0.002). All the patients were subjected to CBNAAT; however, the difference in CBNAAT positivity was not significant between the two groups. At 6 months follow-up, only 3.2% of HIV positive patients remained sputum smear positive, while 2.4% of HIV negative patients remained sputum smear positive, which were declared as treatment failure. This difference at 6 months follow-up was not considered to be statistically significant (p >0.001) (Table 4).

Table 2: Shows the distribution of extrapulmonary TB sites among the study population

Type of extrapulmonary TB	*HIV positive*		*HIV negative*	
	N	*%*	*N*	*%*
Pleural effusion	21	23.1	14	46.6
TB meningitis	5	5.5	1	3.3
TB lymphadenopathy	14	15.3	4	13.3
Abdominal TB	49	53.8	10	33.3
Pott's spine	1	1.1	1	3.3
Other mixed forms	1	1.1	0	0.0
Total	91	100	30	100

60.3% of HIV positive pulmonary TB patients and 83.0% of non-HIV pulmonary TB patients were declared as cured (p <0.001). Among extrapulmonary TB patients, 69.2% HIV positive patients and 80.0% non-HIV patients were declared treatment complete (p<0.001). Lost to follow-up was significantly more in HIV positive patients in both pulmonary and extrapulmonary TB (p = 0.006). More deaths were observed in HIV positive patients in both pulmonary (22.2 vs 7.7%) and extrapulmonary TB (18.7 vs 10.0%) (p = 0.006) (Table 5).

The mean CD4 count among HIV positive patients increased from 194.85 at baseline to 288.18 at 6 months follow up and this increase in CD4 count among HIV positive patients was found to be statistically significant (p<0.001) (Figure 2).

Table 3: Shows the distribution of cases according to treatment outcome

Outcome	*HIV-positive*		*HIV-negative*		*p-value*
	N	*%*	*N*	*%*	
Treatment success*	101	65.5	195	82.6	<0.001
Died	31	20.1	19	8.0	0.002 (S)
Lost to follow up	20	13.0	17	7.2	
Treatment failure	2	1.3	5	2.1	
Total	154	100	236	100	

Table 4: Shows distribution of pulmonary TB patients according to sputum smear status at baseline and at the end of treatment in study group

Duration	*Sputum smear for AFB*	*HIV-positive (N = 63)*		*HIV-negative (N = 206)*		*p-value*
		N	*%*	*N*	*%*	
Baseline	Positive	25	39.7	43	20.8	0.002(S)
	Negative	38	60.3	163	79.1	
At the 6 months	Positive	2	3.2	5	2.4	0.529(NS)
	Negative	39	61.9	163	79.1	

Table 5: Shows the outcome according to type of TB

Outcome	*Type of TB*	*HIV-positive*		*HIV-negative*		*p-value*
		N	%	N	%	
Cured	-	38/63	60.3	171/206	83.0	<0.001(S)
Treatment Complete	-	63/91	69.2	24/30	80.0	<0.001(S)
Treatment failure	Pulmonary	2/63	3.2	5/206	2.4	-
	Extrapulmonary	0	0	0/30	0	
Lost to follow up	Pulmonary	9/63	14.3	15/206	7.2	0.006(S)
	Extrapulmonary	11/91	12.1	2/30	6.6	
Died	Pulmonary	14/63	22.2	16/206	7.7	0.006(S)
	Extrapulmonary	17/91	18.7	3/30	10.0	

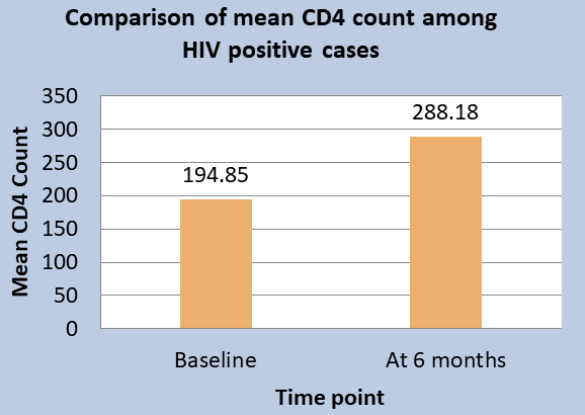


Figure 2: Compares mean CD4 count among HIV positive cases at baseline and at 6 months of treatment

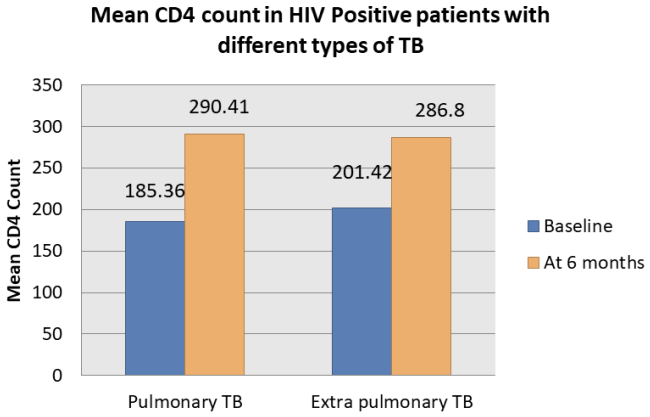


Figure 3: Compares the mean CD4 count in HIV positive patients having different types of TB

The mean CD4 count in pulmonary TB patients increased from 185.36 at baseline to 290.41 at 6 months follow up and this increase was found to be significant (p=0.007). Similarly, the mean CD4 count in extra pulmonary TB patients increased from 201.42 at baseline to 286.8 at 6 months follow up and this increase was also found to be significant (p=0.006) (figure 3).

The mean CD4 count among patients declared cured was found to increase from 185.86 to 294.92 at 6 months ($p = 0.003$). Among treatment-complete patients, CD4 count increased from 202.24 to 286.80 and this increase was also found significant ($p = 0.002$) (Table 6).

Table 6: Shows the mean CD4 count according to treatment outcome in HIV seropositive TB patients

Outcome	*CD4 count (Mean ± SD)*		*p-value*
	Baseline	*At 6 months*	
Cured	185.86 ± 158.36	294.92 ± 243.32	0.003(S)
Treatment complete	202.24 ± 171.68	286.80 ± 196.49	0.002(S)
Died	131.70 ± 98.32	-	-
Lost to follow up	288.75 ± 131.10	-	-
Treatment failure	202.00 ± 209.30	250.00 ± 197.98	0.835(NS)

Discussion

In the present study, the mean age of HIV negative patients (38.48 years) was significantly higher than HIV-positive patients (35.83years). This was also observed by Gupta PR[20] *et al.*, i.e., 37.8 ± 5.9 years in HIV negatives and 32.4 ± 4.0 years in HIV positives TB patients. In this study, most of the TB patients were males in the HIV-positive (74%) and HIV-negative group (68.3%). Similar findings were observed by Vashishtha *et al.*[21] (83% in HIV positives and 58% in HIV negatives) and Gupta PR *et al.*[20] (92.5% in HIV positives and 78% in HIV negatives).

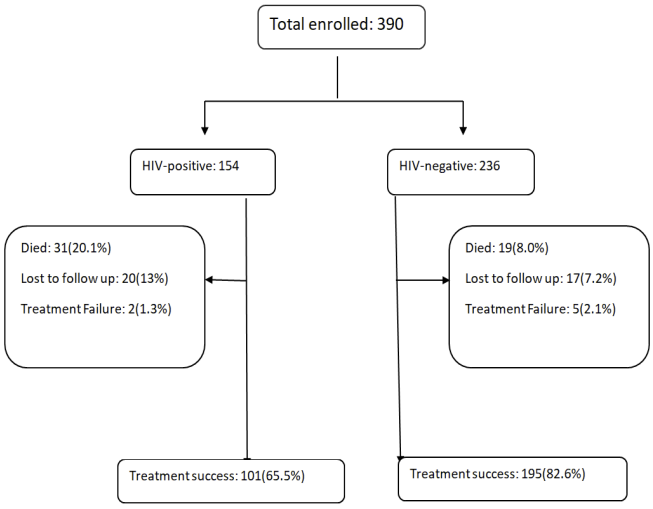
Among HIV negative patients, in the present study, pulmonary TB was more common (87.2%), while among HIV positive patients, extrapulmonary TB was more common (59.1%), this difference was statistically significant. Similarly, Vashishtha *et al.*[21] found that extrapulmonary involvement and dissemination were significantly higher in patients with HIV infection(40.7% among HIV positives as compared to 23.2% among HIV negatives). Kavya[22] *et al.* also found that out of 100 HIV positive patients 65 had extrapulmonary TB. Same findings were also observed by Gupta PR[20] *et al.* (Pulmonary TB alone in 94% among HIV negative patients). Vishal C

Soyam[23] *et al.* also found that 53.8% of HIV positive patients had extrapulmonary TB and 57.9% of HIV negative patients had Pulmonary TB.

Treatment outcome in the present study is shown in Flow chart 1.

The treatment success rate (cured and treatment completed) was significantly higher in non- HIV patients as compared with HIV-positive patients (82.6 vs 65.5%) and this difference was statistically significant (p<0.001). The death rate (20.1 vs 8.0%) and lost to follow-up (13.0 vs 7.2%) were higher in HIV positive individuals, this difference reaching statistically significant (*p-value*=0.002). Vashishtha[21] *et al.* similarly found that treatment success, i.e., cured and treatment completed in 76·7% of the HIV-positive and 93·5% of the non-HIV patients after DOTS (p<0 ·001). Nahid *Et al.*[24] also observed 74.24% treatment success after DOTS among 264 HIV positive patients, while 83% treatment success among 436 HIV negative patients. Mortality rates were also significantly higher among HIV positive patients (14.8 vs 3.9%) in this study. Higher treatment success rate in HIV-negative and higher mortality rate in HIV-positive patients in the present study are also favoured by Sterling TR[25] *et al.* Shastri *et al.*[26] observed that among 51966 non-HIV and 5079 HIV positive patients with TB, treatment success rates were almost similar between both groups. Death rates were expectedly higher in the TB with HIV patient group. However, rates of default (8.8 vs 4.4%) and treatment failure (2.4 vs 0.5%) were higher among HIV negative TB patients. This could be due to large differences in the number of patients enrolled in the two groups.

There was a significantly higher death rate (15.7 vs 7.1%) among the HIV co-infected TB patients. Worldwide, TB-associated mortality in HIV co-infected patients is reported to be nearly three times higher than in patients with TB alone. There are multiple explanations for the increase in death rate in patients who are co-infected. The severity of immune suppression also has a significant impact on the location and extent of TB, the difficulty of diagnosis, and delay in treatment initiation, all of which contribute to higher mortality rates. The likely cause for higher default rates among co-infected patients includes poor knowledge regarding disease, loss of daily wages, patient mis-information about the pattern of TB or outcome of ATT, adverse effects of drugs, increased number of pills, behavioural disorders, addictions, habitual defaulters and intercurrent opportunistic infections, etc.



Flow chart 1: Treatment outcome in the present study

Above comparative analysis of treatment outcome among 'HIV positive' and 'HIV negative' patients in various published studies, clearly indicates that, largely, there is no difference in outcome between daily and intermittent regimens (Tables 7 & 8).

Among HIV positive pulmonary TB patients in the present study, 39.7% were microbiological confirmed, while among HIV negative pulmonary TB patients, 20.8% were microbiological confirmed on smear microscopy and this variation was found to be statistically significant. At 6 months follow-up, sputum positivity rate declined to single numbers in both groups, but that difference was not statistically significant. Contrarily, Vishal C Soyam *et al.*[23] observed that among HIV positive TB patients, 66.6% were sputum positive, while among non-HIV TB patients, 85.1% were sputum positive. Gupta PR *et al.*[20] also observed 37.5% smear positive among HIV positive pulmonary TB patients and 75.88% smear positive patients among HIV negative pulmonary TB patients. Chennaveerappa PK and colleagues[27] also noted a reduced smear positivity in patients who were HIV positive when compared to those who were HIV negative (61.9 vs 71.8%). Similarly, Vashishtha *et al.*[21] observed more sputum positive among non-HIV patients than HIV positive patients (86.6 vs 51.6%). This difference could be clarified by the fact that in our study, HIV patients were of a relatively younger age group (15–45 years age group having HIV positive 82.4 vs 68.7% in HIV negative) with a relatively high CD4 count (less degree of immune suppression), so more chances of smear positivity among HIV positive patients. Another explanation could be a large difference in the total number of cases enrolled in the two groups.

Mean CD4 count among HIV positive patients significantly increased from 194.85 at baseline to 288.18 at 6 months follow-up. Mean CD4 count in pulmonary TB patients as well as extra pulmonary patients among HIV positives increased at 6 months follow up and this increase was statistically detectable (p <0.001). A trivial rise in CD4 count was observed in treatment failure cases (200 to 250 cells, respectively). This might suggest that a lack of favourable response to anti-TB treatment in these cases is directly related to improvement in CD4 counts. Similarly, Vashishtha[21] *et al.* also observed a significant mean rise in CD4 cell count during follow-up from 194.1 to 330.8 (*p-value* >0.001). A study by

Table 7: Shows the treatment outcome of HIV positive TB patients in comparison to other studies

S. No.	Name of study	Sample size	Outcome			
			Treatment success	Lost to follow up	Treatment failure	Death
1.	Present study	154	101 (65.5%)	20 (13%)	2 (1.3%)	31 (20.1%)
2.	Nahid P *et al.*[24]	264	196 (74.24%)	8 (3.0%)	0	39 (14.8%)
3.	Shastri *et al.*[26]	5079	3776 (74.3%)	226 (4.4%)	23(0.5%)	797 (15.7%)
4.	Chennaveerappa PK *et al.*[27]	41	25 (60.98%)	3 (7.3%)	2 (4.8%)	8 (19.5%)
5.	A. Mohan *et al.*[28]	86	70 (82%)	1 (1%)	1 (1%)	9 (11%)
6.	Vashishtha *et al.*[21]	150	115 (76.7%)	9 (6.0%)	8 (5.3%)	13 (8.7%)
7.	Warkari PD *et al.*[29]	87	69 (79.3%)	8 (9.19%)	0	7 (8.05%)
8.	Narendran Gopalan *et al.*[30]	110	75 (68.1%)	10 (9%)	8 (7.2%)	5 (4.5%)
9.	Pruthu Thekkur *et al.*[31]	961	736 (76.6%)	55 (5.7%)	0	152 (15.8%)
10.	Narendran Gopalan *et al.*[30]	111	89(80.1%)	4(3.6%)	0	4(3.6%)
11.	Narasimhamurthy, *et al.*[32]	377	290(76.9%)	0	0	87(23%)

Kavya[22] *et al.* also observed a statistically significant increase in mean CD4 count among the HIV positives, irrespective of pulmonary or extrapulmonary status. Mean CD4 was 197 cells/µL (ranging from 7–940) counts in patients with PTB prior to introducing ATT and those in patients with EPTB was 192 cells/µl. Following treatment, these were 300 cells/µL and 302 cells/µL, respectively (*p-value* >0.005).

In conclusion, the present study shows the wonderful efficacy and safety of daily DOTS in HIV-negative individuals, supporting its role as an effective treatment strategy. However, outcomes among HIV co-infection with daily DOTS and ART were comparatively poorer than HIV negative TB patients, with lower treatment success and higher mortality and higher lost to follow-up. This could be attributed to the additive effects of the severity of the two diseases. This leads to more concentrated research on the treatment results for these patients, particularly highlighting the importance of adherence and counselling to enhance treatment outcomes.

This study faced several limitations, including a high attrition rate, especially within the HIV-positive group, as well as the loss of follow-up after the initial treatment, which may have impacted the completeness of the data. Such challenges are frequently encountered in resource-limited environments. Moreover, this research was observational, leading to limited control over confounding variables, as indicated by baseline heterogeneity. Given the small number of failure cases, it is challenging to confidently assess the differences between the two groups in this regard. Also, the definitive cause of treatment interruption could not be ascertained in lost-to-follow-up cases. However, despite these limitations, this study supplements information to currently insufficient data on outcomes of DOTS in HIV co-infected patients. The actual situation has also been studied, with inclusion of smear-negative and extrapulmonary patients, simultaneous ART, and NTEP treatment protocol, giving strength to this study.

Table 8: Compares the treatment outcome of HIV negative patients among different studies

S. No.	Study	No. of patients	Outcome			
			Treatment success	Lost to follow up	Treatment failure	Death
1	Present study	240	195 (82.6%)	17 (7.2%)	5 (2.1%)	19 (8.0%)
2.	Nahid, Gonzalez, Rudoy, *et al.*[24]	436	362 (83%)	21 (4.8%)	0	17 (3.9%)
3.	Shastri *et al.*[26]	51966	34,924 (79.9%)	4,557 (8.8%)	1249 (2.4%)	3,670 (7.1)
4.	Chennaveerappa P.K. *et al.*[27]	239	189 (79.1%)	17 (7.1%)	13 (5.4%)	20 (8.3%)
5.	Vashishtha *et al.*[21]	155	145 (93.5%)	4 (2.6%)	4 (2.6%)	2 (1.3%)
6.	Pranab Kumar Mandal *et al.*[33]	43	37 (94.8%)	4 (9.3%)	2 (4.65%)	0
7.	Thorve Swapnil M[34]	36	32 (88.8%)	2 (5.5%)	2 (5.5%)	0
8.	Anwith, *et al.*[35]	42	38 (90.47%)	0	0	4 (9.5%)
9.	Pranab Kumar Mandal *et al.*[33]	40	36 (94.7%)	2 (5%)	2 (5%)	0
10.	Gebrezgabiher *et al.*[36]	1537	1310 (85.2%)	171 (11.1%)	4 (0.3%)	52 (3.4%)
11.	Thorve Swapnil M[34]	35	30 (85.7%)	4 (11.4%)	1 (2.8%)	0
12.	Anwith, *et al.*[35]	39	35 (89.74%)	0	1 (2.6%)	3 (7.7%)

Table 9: Compares mean CD4 counts at baseline and at 6 months of treatment among different studies.

S. No.	*Study*	*No. of patients*	*Mean count at baseline*	*Mean CD4 count at 6 months*
1.	Present study	154	194.85	288.18
2.	Aparna *et al.*[36]	25	653.3	680.48
3.	Vashishtha *et al.*[21]	150	194	330.8
4.	Skogmar *et al.*[37]	71	296	392
5.	C.Wejse *et al.*[38]	71	307	317
6.	Kavya S *et al.*[22]	100	240	336
7.	Dinakar *et al.*[39]	90	170.69	309.27
8.	Narasimhamurthy, *et al.*[32]	377	191.76	298.0

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