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ORIGINAL ARTICLE

Factors Affecting Treatment Outcomes in Rifampicin Sensitive Pulmonary Tuberculosis - HIV Coinfected Patients

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Abstract

Background: Tuberculosis and human immunodeficiency virus (HIV) are synergistic infections which pose a major challenge in management of both the diseases. This study was conducted to see for possible factors that may be significantly associated with treatment outcomes in such patients. Methods: An observational prospective study was conducted among 54 HIV- drug sensitive pulmonary tuberculosis patients in a tertiary care hospital. Detailed history was taken, clinical examination and investigations was done. Patients were followed up till the completion of antitubercular treatment. Result: Out of 54 patients, 35 (64.8%) patients completed the RNTCP definition for cured/ treatment completed while 19 (35.2%) patients had unsuccessful outcomes. 44 (81.5%) patients were male. Cough and fever were the most common symptom, presented by all the patients. Patients with low CD4 count (d"200 cells/mm^3) and also patients with platelet count (<1.5 lakh/mm^2) were significantly associated with unsuccessful outcome respectively. Out of 31 patients who never had history of antituberculosis treatment (ATT), 26 (83.9%) patients were significantly associated with successful outcome. Patients who never received ATT and absence of cavity on chest X - Ray were significantly associated with a successful outcome. Patients with no cavity on chest X - Ray and CD4 count > 200 cells/mm^3 were significantly associated with successful outcomes. Out of 17 patients with more extensive lesion on chest X - Ray and CD4 count d" 200 cells/mm^3, 10 (58.8%) patients were significantly associated unsuccessful outcome. Patients who had BMI <18.5 kg/m^2 and CD4 count <200 cells/mm^3 were significantly associated unsuccessful outcome. Conclusion: For an effective management of patients with tuberculosis-HIV coinfection, it is essential to have an earlier diagnosis and timely proper treatment for both the infection to have successful treatment outcome.

Keywords: Antituberculosis treatment, chest X - Ray, CD4 count, cavity

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Introduction

Tuberculosis (TB) is the most common opportunistic infection and cause of mortality among people living with Human immunodeficiency virus (PLHIV), difficult to diagnose and treat owing to challenges related to comorbidity, pill burden, co- toxicity and drug interactions [1].

HIV infected persons have approximately an 18 times greater risk of developing TB than persons without HIV infection [1]. The risk of TB in HIV infected persons continue to increase as HIV disease progresses and CD4 count decreases. While Anti-Retroviral therapy(ART) can substantially decrease the risk of developing TB, the risk always remains higher than that in HIV negative individual. Furthermore, among cured TB survivors with HIV infection, the risk of recurrent TB is also quite high [2].

In the national programme for treatment of TB in India, namely National TB Elimination Programme (NTEP), treatment for drug sensitive TB is for a minimum of 6 months, which may need to be extended under various conditions. Treatment duration of TB in HIV positive patients is unchanged compared to HIV Negative patients [2].

HIV positive patients also require ART for life as there is yet no cure for HIV/ AIDS. With current evidence-based medicine, ART is started whenever HIV positivity is detected, irrespective of their CD4 counts. Patients are also predisposed to other opportunistic infections which may require treatment such as chemoprophylaxis for pneumocystis infection in the form of cotrimoxazole and other drugs. Due to these reasons, adverse effects to drugs and drugs interactions are also more in PLHIV patients, as there is increased pill burden for longer time. Current trends indicate increased mortality for HIV positive patients developing MDR-TB. But there remains an unanswered question regarding the outcome of HIV positive patients with drug sensitive TB who are taking proper ATT along with other requisite measures like ART, prophylaxis for other opportunistic infections and treatment for other pathologies arising due to HIV [2].

0.93 lakh tuberculosis cases in India were attributed to HIV. Treatment of TB-HIV co-infection is a great challenge, more so in

developing countries where TB is the commonest opportunistic infection in HIV infected patients [3].

This study was conducted to study the outcome of anti TB treatment in HIV positive patients who were rifampicin sensitive i.e., suffering from drug sensitive TB, to see whether HIV positivity in absence of drug-resistant TB is itself an adverse factor and whether there are certain baseline parameters or predisposing factors in such patients warranting special attention due to unfavourable prognosis.

Material & Methods

Study Population

All HIV-pulmonary tuberculosis co infected patients enrolled in OPD and indoor in our tertiary care hospital who tested sensitive to Rifampicin on sputum CBNAAT and met the inclusion and exclusion criteria were taken up in the study group.

Study Design

It was an observational prospective study.

Sample Size

The average number of HIV-TB patients initiated on ATT over the last 4 quarter at our OPD and attached ICTC was 22 with a prevalence of 2% [1].

To calculate the sample size the following formula was used

N=4pq/d2

p = prevalence from previous studies or expected prevalence.

q= 1-p

d= allowable error that was 5-20% of maximum p (0.5). For our study, p=0.02.

So, q = 1-0.02= 0.98

Allowable error d was taken as 8% of 0.5 N =49 So, sample size was 49.

Keeping in mind, the prevalence of extra pulmonary TB cases, MDR TB cases and dropout rates, the sample size in this study was taken as 30.

Study period

Intake period started from 1st September 2017 to 30 September 2018. All patients were followed up till completion of their antitubercular treatment.

Inclusion criteria

1) All HIV Positive- TB co-infected patients tested sensitive to Rifampicin under NTEP.
2) All patients who gave written consent & showed willingness to pursue follow-up upto tuberculosis treatment outcome.

Exclusion criteria

1) Extra pulmonary TB patients.
2) Pregnant patients.
3) Age less than 14 years.
4) Any drug resistance.
5) Diabetes mellitus patients.
6) Patient not giving consent

Consent and ethical consideration

Ethical approval for this study was obtained from the Institutional Human Ethics Committee.

Sampling technique

Every consecutive patient who fulfilled our inclusion and exclusion criteria.

Data collection technique and tools

Informed written consent was taken from the patients who fulfilled the inclusion criteria for their inclusion in study & willingness to undergo diagnostic evaluation.

Methodology

1. History, clinical examination & pretreatment evaluation.
2. Personal habits.
3. Treatment history.

↓

Investigation-

1. Body weight, height, Body mass index.
2. CBC, LFT, KFT, blood sugar (Fasting and Random).
3. Sputum test for Acid fast bacilli.
4. Chest X-ray.
5. Baseline CD4 count.

Chest X - Ray findings were classified as per the guidelines of National Tuberculosis Association of USA as minimal, moderately advanced and far advanced lesions [4].

Minimal and moderately advanced lesions were grouped in less extensive group and far advanced lesions in more extensive group. At the end of the study, patients were divided into various groups based on possible outcomes [2] and compared for possible significant factors.

Statistical Analysis

Descriptive statistics was analyzed using the SPSS version 18.0 software. Continuous variables were presented as mean (SD) or median if the data was skewed. Chi-square test was used for comparison of nominal categorical data between the groups. A p value less than 0.05 was taken to indicate a statistically significant difference.

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Results

A total of 54 patients fulfilling inclusion and exclusion criteria of this study and providing informed consent were included in the study in the prescribed time period. Out of them, 4 (7.4%) patients were lost to follow up, 10 (18.5%) patients expired, and 5 (9.3%) patients had a treatment failure in the form of microbiological positivity, all of them were termed under unsuccessful outcome. 35 (64.8%) patients completed the RNTCP definition for cured/ treatment completed and these were grouped under successful outcomes.

For the purpose of further analysis, the patients in this study were divided in two groups based on their final outcomes.

Group A - Patients with successful outcomes which includes

treatment completed and cured (35 patients)

Group B - patients with unsuccessful outcomes which includes lost to follow up, treatment failure, death (19 patients).

There were 28 (80%) male and 7(20%) female patients in group A while 16 (84.2%) male and 3 (15.8%) female patients belonged to group B. 30 (65.2%) and 16 (34.8%) patients with BMI <18.5 kg/m^2 belonged to group A and B respectively. In this study out of 54 patients, cough and fever were the most common symptoms 54 (100%) and expectoration was the second most common symptom in 50 (92.6%) while hemoptysis was the least common 4 (7.4%).

As shown in table-1, out of 29 patients with CD4 count d" 200 cells/mm^3, 15 (51.8%) patients were significantly associated (p value - 0.006) with unsuccessful outcome.

Table 1: Comparison of treatment outcomes according to baseline CD4 count

CD4 count(cells/mm^3)	Group A	Group B	P value
≤200	14 (48.3%)	15 (51.8%)	0.006
>200	21 (84%)	4 (16%)	

In this study it was observed that reduced platelet count (<1.5 lakh/mm^2) at baseline was significantly associated (p value-0.045) with unsuccessful outcome as can be seen in table-2.

Table 2: Comparison of treatment outcomes according to biochemical parameters of patients

Biochemical parameters	Group A No. (%)	Group B No. (%)	p value
Hb (<11g/dl)			
Reduced	23 (63.9%)	13 (36.1%)	0.840
Normal	12 (66.7%)	6 (33.3%)	
TLC (cells/mm^2)			
Reduced(<4000)	2 (33.3%)	4 (66.7%)	0.086
Normal(4000-11000)	22 (71%)	9 (29%)	0.271
Increased(>11000)	11 (64.7%)	6 (35.3%)	0.990
Platelet (lakh/$mm^{2)}$			
Reduced(<1.5 lakh/mm^2)	6 (42.9%)	8 (57.1%)	0.045
Normal(>1.5 lakh/mm^2)	29 (72.5%)	11 (27.5%)	
LFT			
Normal	25 (62.5%)	15 (37.5%)	0.547
Deranged	10 (71.4%)	4 (28.6%)	
KFT			
Normal	30 (68.9%)	14 (31.8%)	0.277
Deranged	5 (50%)	5 (50%)	

As shown in table 3, out of 31 patients who never had history of ATT intake, 26 (83.9%) patients were significantly associated with successful outcome while 5 (16.1%) had unsuccessful outcome while out of 23 patients who had history of ATT intake atleast once, 14 (60.9 %) had unsuccessful outcome while 9 (39.1%) had successful outcome. In this study, patients who were receiving ATT for the first time, were significantly associated with a successful outcome. Out of 18 patients with cavity on chest X - Ray 10 (55.6%) had unsuccessful outcome while out of 36 patients without cavity 27 (75%) had successful outcomes. In this study absence of cavity on chest X - Ray was significantly associated (p value - 0.026) with successful outcomes.

Table 3: Comparison of treatment outcomes according to number of times ATT intake between the groups and baseline presence of cavity on chest X - Ray

Number of times ATT intake	Group A	Group B	P value
Never	26 (83.9)	5 (16.1%)	0.0006
>1	9 (39.1%)	14 (60.9%)	
Chest Xray	Group A	Group B	P value
Cavity present	8 (44.4%)	10 (55.6%)	0.02
Cavity absent	27 (75%)	9 (25%)	

As per table-4, out of 43 patients with no cavity on chest X - Ray and CD4 count > 200 cells/mm^3, 31 (72.1%) were significantly associated with successful outcomes.

Table 4: Comparison of treatment outcomes with presence of cavity or more extensive lesion on chest X - Ray and CD4 count > 200 cells/mm^3 on chest X - Ray

Cavity on Chest xray and CD4 count ≤200 cells/mm^3	Group A	Group B	Total	p-value
Present	4(36.4%)	7(63.6 %)	11(100%)	0.026
Absent	31(72.1%)	12(27.9%)	43(100%)	
More extensive lesion on chest X - Ray and CD4 count ≤ 200 cells/mm^3	Group A	Group B	Total	p-value
Present	7(41.2%)	10(58.8%)	17(100%)	0.0136
Absent	28(75.7%)	9(24.3%)	37(100%)	

Out of 17 patients with more extent of lesion on chest - X - Ray CD4 count d" 200 cells/mm^3, 10 (58.8%) patients were significantly associated unsuccessful outcome as shown in table-5. Unsuccessful outcomes were associated with patients who had extensive lesions on chest X - Ray & CD4 count < 200 cells/mm^3 in this study.

As shown in table 5, in this study out of 25 patients, unsuccessful outcomes were significantly associated (0.016) with patients who had BMI <18.5 kg/m^2 and CD4 count <200 cells/mm^3 in 13 (52%) patients. Significantly successful treatment outcomes were associated in 32(80%) patients who never had taken ATT and CD4 count > 200 cells/mm^3.

Table 5: Comparison of treatment outcomes with patients with BMI <18.5kg/m^2 and CD4 count d"200 cells/$mm^3$and number of times of ATT intake > 1 and CD4 count < 200 cells/mm^3 respectively

BMI <18.5 kg/m^2 & CD4 count ≤200 cells/mm^3	Group A	GROUP B	Total	p-value
Present	12(48%)	13(52%)	25(100%)	0.016
Absent	23(79.3%)	6(20.7%)	29(100%)	
Number of times of ATT taken (≥ 1) and CD4 count ≤ 200 cells/mm^3	Group A	GROUP B	Total	p-value
Present	3(21.4%)	11(78.6%)	14(100%)	0.00007
Absent	32(80%)	8(20%)	40(100%)	

Discussion

The global fight against TB is complicated due to the emergence of

a viral disease, HIV. HIV leads to immunosuppression, predisposing the patients to other infections which ultimately prove fatal. One of the life-threatening infections in HIV patients is Tuberculosis [5].

This study aims to evaluate the treatment outcomes of rifampicin sensitive pulmonary TB-HIV coinfected patients under RNTCP and to study possible factors associated with the various possible outcomes.

Treatment outcomes

In our study out of total 54 patients, 4 (7.4%) patients were lost to follow up, 10 (18.5%) patients expired, and 5 (9.3%) patients had a treatment failure in the form of microbiological positivity, all of them were termed under unsuccessful outcomes (group B) (35.2%). 35 (64.8%) patients completed the RNTCP definition for cured/ treatment completed, and these were grouped under successful outcomes (Group A) (64.8%).

In 2021, out of 35,578 patients PLHIV with diagnosed TB in India, 35709 were registered for treatment, 22632 patients (63.4%) had treatment successful, death were 519 (1.4%), treatment failure were in 137 (0.38%), lost to follow up were 523 (1.5%), treatment regimen changed in 254 (0.71%) patients and 549(1.0%) were not evaluated. In Delhi region, out of 7932 notified tb patients, treatment was successful in 6495 (81.9%) and deaths were 93 (1.2%), lost to follow up in 201 (2.5%), treatment failure in 55 (0.69%) and treatment regimen changed in 119 (1.5%).[1] In comparison, in this study successful outcomes were low. Possible explanation for this could be that being a tertiary referral hospital, patients report at an advance stage of disease.

Most of the patients in this study were in the age group of 30 - d" 40 years (44.4%). Successful outcomes were higher in the patients in the age group 40- 50 years (77.8%).

In the study done by Gautam L. et al, most of the HIV positive patients were in the age group 30-45 years (71.43%, n=275) which is sexually active group [6].

In this study out of 54 patients, 44(81.5%) were males. Most of the patients were males (72.7%) in the study done by Ambadekar et al. [7]. This may be due to males seek treatment earlier and have more family support.

Out of 19 patients with unsuccessful outcomes, 13 had reduced hemoglobin (<11g/dl) in this study. It was observed that 8 patients out of 19 unsuccessful outcomes had reduced platelets count. Kassa Eyuel et al showed that platelet count was another important hematological profile that showed significant difference in almost half of TB patients when the count before initiation of tuberculosis treatment was compared to that of platelet count after completion of the 2 month tuberculosis treatment (p = 0.010) [8].

In this study, patients with CD4 count below 200 cells/mm^3 were significantly associated (p value=0.006) with unsuccessful outcomes compared to patients with CD4 count above 200 cells/mm3. According to the study by Montalvo Raúl et al, all of the patients who died during treatment had a CD4 count <200 cells/mm^3, whereas those who survived, one third, had a CD4 count greater than or equal to 200 cells/mm^3 [9].

Low CD4 cells in HIV-infected persons indicates severely depressed immunity that makes them susceptible to fresh TB infection or reactivation of latent infection and rapid degradation of clinical condition. It has already been established that TB attributed to a six-fold to seven-fold increase of viral load in HIV positive population [10].

In our study, retreatment cases were significantly associated (p value = 0.0006) with unsuccessful outcomes (73.7%) in comparison to new cases outcomes (26.3%). Dheda at el, also concluded that retreatment cases were associated with poor outcome [11].

In this study, absence of cavity on chest X - Ray was significantly associated (p-value=0.026) with successful outcomes. In a study by Perlman *et al*, cavity was observed in 20% [12]. Successful outcomes are more in patients with less extensive lesion on chest X - Ray, may be due to less severe symptoms and better compliance towards nutrition and medications.

Combining the significant factors

In this study successful outcomes were significantly associated (p value=0.026) in patients with no cavity on chest X - Ray and CD4 count >200 cells/mm^3.

Out of 19 patients with unsuccessful outcomes in our study 10 patients had more extensive lesions and CD 4 count d" 200 cells/ mm^3 and the association was statistically significant (p value=0.0136). There are more chances of unsuccessful outcomes in low CD4 counts mainly due to inadequate defence mechanism in the body to fight back against the infection thus aggravating the disease progression [5].

Out of 19 patients with unsuccessful outcomes in this study 13 patients had BMI <18.5 kg/m2 and CD4 count <200 cells/mm^3 and was significantly associated (p value=0.016). Maro L. et.al. concluded in their study among HIV - infected adults with CD4 counts of e"200 cells/ mm^3 living in a high TB prevalence area, low BMI and falling BMI were independently and significantly associated with greater risk of developing TB. These results suggest that malnutrition contributes to HIV- associated TB, and that subjects with BMI < 17 kg/m^2 or a 1-year BMI decrease of e"0.5 kg/m2 have a heightened risk of developing HIV-associated TB [13].

Malnutrition aggravates the risk of infection; low BMI is related to a greater bacillary burden during HIV-associated TB. Low BMI contributes to the development of TB, perhaps by exacerbating HIV-associated deficits in cell- mediated immunity [13].

In this study out of 34 patients with successful treatment (p value=0.00007) outcomes 32 patients had never taken ATT and had CD4 count >200 cells/mm^3.

This suggests that the immuno-competency prevent disease progression and early improvement in health status thus increase chances of successful outcomes in patients of TB-HIV.

Conclusion

It is pertinent for HIV patients with coinfection with tuberculosis to have an earlier diagnosis, maintaining nutritional diet and complete proper treatment for both the infection to improve the immunity and prevent worsening of respiratory symptoms.

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