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Assessment of Determinants Affecting Treatment Outcomes in Rifampicin Sensitive Pulmonary Tuberculosis-HIV Co-infected Patients

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Introduction

Although there have been rapid advances in medical science and technology, Tuberculosis (TB) continues to remain an important public health problem with crippling and alarming figures for morbidity and mortality worldwide, but more in the developing and underdeveloped countries[1].

Human immunodeficiency virus (HIV) leads to immunosuppression, pre-disposing patients to other infections, which ultimately prove to be fatal. One of the life-threatening infections in HIV/AIDS patients is Tuberculosis which is more common, more virulent and more deadly in HIV patients, compared to an immune-competent individual[2].

There are still a large number of people living with HIV (PLHIV) who have tuberculosis but are undiagnosed due to atypical symptoms and signs and low bacillary load. It is critical to bridge this gap. Since TB variably affects PLHIV, it is crucial to have an appropriate prevention programme, earlier diagnosis and adequate treatment[2].

As per the latest India TB report, globally the incidence of HIV positive TB cases was approximately 7,03,000 (6,33,000 - 7,76,000), mortality was 1,87,000 (1,58,000 - 2,18,000). In India, the incidence was 54,000 (46,000 - 63,000), and mortality was 11,000 (9,900 - 13,000)[3].

Even though HIV prevalence among incident cases of TB is low in India when compared to the global prevalence of 12.6%, TB-HIV co-infected patients in absolute numbers are vast. Such numbers give rise to a large number of deaths, and transmissible cases, and a considerable burden on the existing healthcare system[4].

HIV-TB co-infection does not have a good prognosis. HIV itself poses a serious threat for developing drug-resistant TB, which has a poor outcome and HIV infection debilitates the patient further, reducing compliance to antitubercular treatment (ATT).

This study was designed to assess the treatment outcomes in HIV-TB patients who are not drug resistant and to evaluate any possible factors that may be significantly associated with these treatment outcomes.

Material and Methods

Study design

An observational, prospective study was conducted among rifampicin sensitive pulmonary tuberculosis-HIV co-infected OPD and indoor patients who met the inclusion and exclusion criteria at Rajan Babu Institute for Pulmonary Medicine and Tuberculosis (RBIPMT), GTB Nagar, Delhi and attached Integrated Counselling and testing centre (ICTC) from 1st September 2017 to 30 September 2018, and followed-up till completion of the treatment.

Sample size

The average number of HIV-TB patients who were started on ATT at RBIPMT OPD and attached ICTC over the last year was 22, with a prevalence of 2%[5].

Sample size was calculated by the formula-

$N = 4pq/d^2$

p = prevalence from previous studies or expected prevalence.

q = 1-p

d = allowable error (5 - 20% of p) (0.5).

For this study, p = 0.02, thus q = 1-0.02 = 0.98

Allowable error d was taken as 8% of 0.5

Thus, sample size was 49.

Considering, the prevalence of extra-pulmonary TB cases, multidrug resistant tuberculosis cases and lost to follow-up cases, the sample size was taken as 30.

Inclusion criteria

1. All HIV positive – rifampicin sensitive TB co-infected

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patients.

2. All patients who gave written consent and were willing to follow-up up till completion of TB treatment.

Exclusion criteria

1. Any drug resistance.
2. Extra-pulmonary TB.
3. Age less than 14 years.
4. Diabetes mellitus.
5. Pregnancy.

Consent and Ethical consideration

The study was conducted with approval from the Institutional Human Ethics Committee. Every consecutive patient was included in the study after obtaining an informed, written consent.

Material and Methods

Demographic history and symptoms of the patients were noted, along with their weight at baseline. Patients were followed-up till the end of intensive phase (IP), 2 months into continuation phase (CP), and at end of treatment for:

1. Improvement or same/worsening of symptoms.
2. Change in weight.
3. Sputum smear status.

At the end of the study, patients were divided into various groups based on possible treatment outcomes[2] and compared for possible significant factors.

Statistical Analysis

SPSS version 18.0 software was used to analyse descriptive studies. If data was skewed, continuous variables were presented as mean (SD) or median. Chi-squared test was used to compare nominal categorical data between the groups. P value < 0.05 was considered as a statistical significant difference.

Results

A total of 54 patients included in the study, were divided into two groups; group A who had successful outcomes included 35 patients and group B comprised of 19 patients who had unsuccessful outcomes (lost to follow-up, treatment failure and death).

Most patients 24 (44.4%) were in the age group of 30 - 40 years. 44 (81.5%) were male and 10 (18.5%) were female.

Out of total 54 patients who were enrolled at the beginning of study, 4 patients were lost to follow-up. So, further analysis was done on 50 patients. Out of 50, six patients died before the first follow-up at end of IP. Out of the 44 remaining three patients died before the second follow-up at mid CP. Out of 41 patients remaining, 1 patient died before the final follow-up at end of CP.

As shown in Table I, weight was increased in 59.1%, 61%, and 62.5% patients at end IP, mid CP, at end of CP respectively. There was a significant association of increase in weight with successful outcomes at end IP.

Table I: Comparison of weight (kg) between the groups at each follow-up compared to baseline.

Weight (kg) at each follow-up	No. of patients N = 54	Group A	Group B	p-value
	No. (%)	No. (%)	No. (%)	
At the end of IP	N = 44	35	9	
Reduced or same	18 (40.9%)	10 (55.6%)	8 (44.4%)	**0.001**
Increased	26 (59.1%)	25 (96.2%)	1 (3.8%)	
At mid CP	N = 41	35	6	
Reduced or same	16 (39%)	10 (62.5%)	6 (37.5%)	Not applicable
Increased	25 (61%)	25 (100%)	0	
At the end of treatment	N = 40	35	5	
Reduced or same	15 (37.5%)	10 (66.7%)	5 (33.3%)	Not applicable

As shown in Table II there was significant association of improvement of symptoms at end IP and mid CP with successful outcomes.

Table II: Comparison of symptoms between the groups at each follow-up compared to baseline.

Symptoms at each follow-up	No. of patients N = 54	Group A	Group B	p value
	No. (%)	No. (%)	No. (%)	
At the end of IP	N = 44	35	9	
Improved	22 (50%)	21 (95.5%)	1 (4.5%)	**0.008**
Same or worsen	22 (50%)	14 (63.6%)	8 (36.4%)	
At mid CP	N = 41	35	6	
Improved	33 (80.5%)	32 (97%)	1 (3%)	**0.00002**
Same or worsen	8 (19.5%)	3 (37.5%)	5 (62.5%)	
At the end of treatment	N = 40	35	5	
Improved	35 (87.5%)	35 (100%)	0	Not applicable
Same or worsen	5 (12.5%)	0	5 (100%)	
Increased	25 (62.5%)	25 (100%)	0	

There was a significant association of (reduced/same)

weight and sputum smear positive status at end of IP with unsuccessful outcomes (Table III).

Table III: Comparison of (reduced/same) weight and sputum smear positive status between the groups at each follow-up.

(Reduced/same) Weight (kg) and sputum smear positive status at each follow-up	No. of patients N = 54	Group A	Group B	p value
	No. (%)	No. (%)	No. (%)	
At the end of IP	N = 44	35	9	
Present	11 (25%)	3 (27.3%)	8 (72.7%)	**0.000001**
Absent	33 (75%)	32 (97%)	1 (3.0%)	
At mid CP	N = 41	35	6	
Present	4 (9.8%)	0	4 (100%)	Not applicable
Absent	37 (90.2%)	35 (94.6%)	2 (5.4%)	
At the end of treatment	N = 40	35	5	
Present	5 (12.5%)	0	5 (100%)	Not applicable
Absent	35 (87.5%)	35 (100%)	0	

In this study, there was a significant association of (reduced/same) weight and symptoms of patients (worsened/same) at the end of IP and mid CP with unsuccessful outcomes (Table IV).

Table IV: Comparison of reduced/same weight and worsened/same symptoms of patients between the groups at each follow-up.

(Reduced/ same) Weight(kg) and symptoms of patients (worsened/ same) at each follow-up	No. of patients N = 54	Group A	Group B	p value
	No. (%)	No. (%)	No. (%)	
At the end of IP	N = 44	35	9	
Present	14	6	8	**0.00003**
Absent	30	29	1	
At mid CP	N = 41	35	6	
Present	6	1	5	**0.0001**
Absent	35	34	1	
At the end of treatment	N = 40	35	5	
Present	5	0	5	Not applicable
Absent	35	35	0	

There was a significant association of sputum positive status and symptoms of patients (worsened/same) at end of IP (first follow-up) with unsuccessful outcomes (Table V).

Table V: Comparison of sputum positive status and worsened/same symptoms of patients between the groups at each follow-up.

Sputum positive status and symptoms of patients (worsened/same) at each follow-up	No. of patients N = 54	Group A	Group B	p value
At the end of IP	N = 44	35	9	
Present	15	7	8	**0.00010**
Absent	29	28	1	
At mid CP	N = 41	35	6	
Present	4	0	4	Not applicable
Absent	37	35	2	
At the end of treatment	N = 40	35	5	
Present	5	0	5	Not applicable
Absent	35	35	0	

Discussion

Current trends indicate an increased mortality for HIV positive patients developing multi drug resistant-TB. But there remains an unanswered question regarding the outcome of HIV positive patients with drug sensitive TB taking proper ATT.

It is seen that HIV-TB co-infection is an important public health problem, with poor prognosis; also, HIV is an independent risk factor for drug resistant- TB, which has a uniformly poor prognosis; and HIV is a risk factor for default to treatment[6].

This study was conducted to evaluate the effects of factors at the end of intensive phase, 2 months into continuation phase and end of continuation phase on treatment outcomes of rifampicin sensitive pulmonary TB-HIV co-infected patients under RNTCP.

In this study successful outcomes were seen in 64.8% of patients and unsuccessful outcomes in 35.2% patients. 75.9% patients were less than 40 years of age. 44 patients were male and 10 patients were female. In the study done by Kamath *et al*, HIV-TB co-infection was present in 61.3% patients in age group 31 - 45 years, and 75.3% among males, similar to our study[7].

Follow-up: Out of total 54 patients who were enrolled, 4 patients were lost to follow-up. 6 patients died before the first follow-up at end IP and 3 patients died before the second follow-up at mid CP and 1 patient expired before the final follow-up at end CP.

Comparison of different parameters at all the follow-up: On comparison of weight between the groups across the time period of follow-up, weight was increased in

59.1%, 61%, and 62.5% patients at end IP, mid CP and at the end of treatment, respectively. There was a significant association (p value = 0.001) of increase in weight at end IP with successful outcomes. Montalvo *et al* stated in their study that TB-HIV co-infected patients who died during TB treatment lost weight ($p < 0.001$) while who survived, gained weight ($p < 0.001$)[8].

Wasting occurs frequently during HIV infection and increases with disease progression. As malnutrition is common among HIV-infected individuals, especially where there is co-infection with TB, bioimpedance analysis might be a good approach to prevent deaths among patients with the TB-HIV co-infection[8].

According to our study, there was a significant association of improvement in symptoms at end IP (p value = 0.008) and mid CP (p value = 0.00002) with successful outcomes.

In our study, sputum smear was negative in majority of patients at all the follow-ups. There was a significant (p = 0.00009) association of negative sputum smear at mid CP with successful outcomes.

In a study by Tweya *et al*, there was poorer TB treatment outcome in fifty six per cent patients who had sputum smear positive PTB-HIV co-infection adjusting for gender, age and year of TB registration[9]. This may be due to better treatment compliance and health status which subsequently aid in improvement of symptoms and radiological involvement due to reduced bacillary load.

In our study, there was a significant association (p value = 0.000001) of (reduced/same) weight and sputum smear positive status at end of IP with unsuccessful outcomes. In a study by Krapp *et al* unsuccessful outcome was independently associated with an initial smear 2+ (odds ratio [OR] 2.46, 95% CI 1.14 - 5.31), a positive smear at month 2 (OR 4.0, 95% CI 1.30 - 12.31) and body weight gain) 5% at end of treatment (OR 2.35, 95% CI 1.17 - 4.72)[10].

There was a significant association of (reduced/same) weight and symptoms of patients (worsened/same) at end of IP (p value = 0.00003) and mid CP (p value = 0.0001) with unsuccessful outcomes in our study.

Also, there was a significant association (p value = 0.00010) of sputum positive status and symptoms of patients (worsened/same) at end of IP (first follow-up).

During follow-up, most of these patients had improvement in symptoms, increase in weight and sputum smear status was negative were associated with successful outcomes.

Majority of patients who had unsuccessful outcomes during follow-up, had worsening in symptoms, decrease in weight and sputum smear status remained positive.

Conclusion

Tuberculosis and HIV co-infection impacts patient health adversely and simultaneous treatment of both diseases poses a serious challenge to the healthcare system and patients' wellbeing. Detection of worsening of symptoms, smear status and intervening at the earliest with proper counselling for an adequate nutritional diet at each follow-up can help in improving outcomes in such patients.

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