Original Article

Impact of TB-HIV collaborative activities on case fatality among HIV-infected Tuberculosis patients in Gujarat, INDIA

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DOI : 10.5455/jrmds.2014211

ABSTRACT

Background: Tuberculosis (TB) control efforts have been challenged by deadly interaction of TB and HIV (Human Immunodeficiency Virus) epidemics. To address this challenge in India, all TB patients are routinely offered HIV testing and HIV positive TB patients are provided CPT (Cotrimoxazole Prophylaxis Therapy) and ART (Anti-Retroviral Treatment) as part of TB/HIV collaborative activities.

Objective: To study the impact of TB/HIV collaborative activities on case-fatality among HIV infected patients with tuberculosis.

Methods: All TB registers maintained under National TB programme (RNTCP) in Gujarat were reviewed and data on HIV testing, ART, CPT and TB treatment outcomes were retrieved for all the TB patients registered in 2010.

Results: Among 77,839 registered TB patients, 59,638 (75%) were ascertained for HIV status and 2,893 (4%) were HIV infected. Among those HIV infected TB patients, 95% received CPT and 68% received ART during TB treatment. Case fatality among patients who received both CPT and ART was 10% compared to 37% among those didn't receive both.

Conclusion: TB-HIV collaborative activities reduced mortality among HIV infected TB patients under program condition in Gujarat. The programme needs to sustain efforts of collaborative interventions to improve care for such co-infected patients. Moreover, future TB-HIV collaborative efforts should focus on early diagnosis of HIV and TB and prompt initiation of ART.

Keywords: TB-HIV collaboration, Case-fatality, RNTCP, ART, CPT, Gujarat

INTRODUCTION

Mycobacterium Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) infection continue as major public health challenges in India[1,2]. India had an estimated 2.5 million incident TB cases in 2011 that accounted for around fourth of an estimated all TB cases worldwide[1,3]. Among TB cases, 94,000 patients are estimated to be infected with HIV [3].Estimated number of people living with HIV (PLHIV) in India is 2.4 million[4].Active TB disease is the commonest opportunistic infection and also leading cause of mortality among people living with HIV(PLHIV) [1,5]. The World Health Organization (WHO) had launched TB/HIV collaborative activities in 2004 and developed guidelines for management of HIV-TB patients. One of the important recommendation of guideline is provision of Antiretroviral treatment (ART) and Cotrimoxazole Prophylaxis Therapy (CPT) to HIV-infected TB patients[1,5,6].

Cotrimoxazole is a broad spectrum antibiotic and cost effective intervention given routinely for prevention of opportunistic infections and also has been demonstrated to be effective to reduce mortality in TB

and in other opportunistic infections among PLHIV.[5,7,8] In India, primary prevention with Cotrimoxazole has been recommended by the National AIDS Control Programme (NACP) for all HIV-infected patients with WHO Clinical Stage III and IV [8].

ART reduces morbidity and mortality in people living with HIV/AIDS[5,6,9,10]. India has made free ART widely available through a growing treatment network of ART Centers and Link ART Centers nationwide. For HIV-TB co-infected patients, revised Indian guideline for initiation of ART recommends to start ART irrespective of CD4 count and type of tuberculosis[6].

Based on the framework of WHO TB/HIV collaborative activities, RNTCP launched intensified TB-HIV package in India in 2008 in a phased manner. Among the major activities of Intensified TB-HIV package are to offer voluntary HIV testing to all registered TB patients and to deliver WHO recommended intervention of ART and CPT to all known HIV-TB patients.

The present study evaluated impact of ART and CPT provision to HIV infected TB patients on their TB treatment outcome. We also studied the risk factors associated with case-fatality among HIV-TB patients under programmatic conditions.

MATERIAL AND METHODS

Study design

A retrospective cohort study was conducted to review the records of HIV infected TB patients registered for anti-TB treatment under RNTCP Gujarat in 2010.

Setting

Gujarat state is situated in the western cost of India with around 60 million population in 2010. The state has 26 districts and 30 reporting units under RNTCP. The state has moderate prevalence (<1% HIV prevalence in ANC attendees and >5% HIV prevalence in high risk group) of HIV[4]. It was the first moderate HIV prevalence state to implement Intensified TB-HIV package in India since 2009. All registered TB patients in Gujarat are offered voluntary HIV counseling and testing and TB patients found HIV reactive referred to nearest ART center for initiation of ART and CPT. Free ART is provided at 24 ART centers and 36 Link ART Centers in their respective districts. These service delivery sites under National AIDS Control Program of India (NACP) follow the national guidelines for counseling, testing, care and treatment of PLHIV[6,11].

Study population

All HIV-TB patients registered under RNTCP in the Gujarat state from 1st January to 31st December 2010 were included in study.

Data variable and data collection tool

Data on age, sex, site of disease, type of TB, history of anti-TB treatment, HIV testing, provision of CPT and ART were collected from TB treatment registers routinely maintained under the programme.

Definitions

Standard definitions used under Revised National TB Control Programme (RNTCP) were adopted to categorize patients for type of TB and TB treatment outcomes [12].

Data analysis and management

De-identified data was entered in Epi-info at district level that was compiled and analyzed at state level. Data were analyzed using Epi Info [TM] 3.3.2 (Centers for Disease Control and Prevention, Atlanta, USA). Any potential association of unfavorable outcome (Death/Default/Failure) was explored with independent variables i.e. provision of CPT and/or ART. Chi square test was used as a test of significance. P value less than 0.05 was considered as a level of significance.

Ethical issues

The administrative approval was obtained after review of the protocol by the State TB Cell, Department of Health and Family Welfare, Government of Gujarat. The study was done as a part of routine evaluation of implementation of programme. Electronic databases created for this analysis were stripped of personal health identifiers and maintained securely.

RESULTS

Total 77,839 TB patients were registered under RNTCP in Gujarat from 1st January 2010 to 31st December 2010. Among them, 58,638 (75.3%) had known HIV status and 2,893 (3.7%) were HIV

reactive. Characteristics of HIV-TB patients are shown in Table 1. Three out of four HIV-TB co-infected patients were male. Median age of patients was 35 years with around two third between the age of 25 and 46 years. Out of the 2,893 HIV-TB patients, 1,638 (57%) had pulmonary TB, while 1,255 (43%) had extra-pulmonary TB. Among pulmonary TB, 63% were sputum positive TB and 37% were sputum negative TB. Out of total co-infected patients, 73% were newly diagnosed TB patients and 27% were previously treated TB patients. 68% co-infected patients received ART and 95% HIV-TB patients received CPT, while 3% neither received CPT nor ART during TB treatment.

Table 1: Characteristic of HIV-TB patients, Gujarat, India, 2010, N = 2893

Characteristic	Subcategory	N (%)
Sex	Male	2119 (73)
	Female	774 (27)
Age group	Below 15 years	141 (5)
	15-64 years	2720 (94)
	Above 65years	32 (1)
Type of TB	Pulmonary	1638 (57)
	Extrapulmonary	1255 (43)
Subtype of pulmonary TB	Smear positive TB	1031 (63)
	Smear negative TB	607 (37)
History of TB	New Patients	2126 (73)
	Previously treated Patients	767 (27)
CPT provision during TB treatment	Yes	2744 (95)
	No	149 (5)
ART provision during TB treatment	Yes	1964 (68)
	No	929 (32)
Both CPT & ART provision during TB treatment	Yes	1912 (66)
	No	97 (3)

HIV = Human immunodeficiency virus; TB = Tuberculosis; CPT = Cotrimoxazole prophylaxis therapy; ART = Antiretroviral therapy

TB treatment Outcomes

TB Treatment outcome were available for all 2,893 HIV-TB co-infected patients (Table 2). Out of 2,893 HIV-TB co-infected patients, 2,188 (75%) were successfully treated (24% cured and 51% treatment completed), while 25% unsuccessfully treated (391(14%) died, 233(8%) defaulted, and 42(2%) treatment failure). Successful treatment outcome was significantly more among extra-pulmonary TB cases (81%) as compared to pulmonary TB cases(p<0.001). Among pulmonary TB, treatment success rate was significantly higher among smear negative patients (77.8%) as compared to smear positive TB patients (68.2%) (p<0.001). Similarly, successful treatment outcome was significantly higher among new cases (79.8%) as compared to previously treated TB cases (64%) (p<0.001).

Case-fatality

Total 391(14%) HIV-TB co-infected patients died during TB treatment in 2010. Risk factors associated with case-fatality are shown in Table 3. HIV-TB co-infected pulmonary cases had higher case fatality (16%) than extra-pulmonary TB cases (11%) (OR-1.56, 95% CI 1.24-1.95, p<0.001). Also, 'Previously treated TB patients' had higher case fatality (16%) compared to newly diagnosed TB patients (13%) (OR-0.75, 95%CI 0.6-0.95, p=0.017). The death was higher among patients who did not receive CPT and/or ART as compared to those who received it. Patients who had not received CPT had significantly higher death rate (28%) as compared to those who received CPT (13%) (p<0.001). Similarly, 21% death occurred among patients who were not provided ART during TB treatment as compared to 10% among those who were provided ART (OR 0.43, 95% CI 0.35-0.54, p<0.001). Patients who did not received both CPT and ART during TB treatment; case-fatality was significantly higher (37%) as compared to patients who received both CPT and ART (OR 0.19, 95% CI 0.12- 0.29, p<0.001).

DISCUSSION

We observed a high HIV testing rate among registered TB patients and high CPT administration rate among HIV/TB co-infected patients. AndART could be started in more than two-third of HIV-TB patients, in short span of implementation of revised strategy of initiation of ART. Study observed high death rate (21%) among HIV infected TB patients who were not provided ART during TB treatment as compared to those who were provided ART in program condition in Gujarat.

This was first attempt to evaluate the effect of TB/HIV collaborative activities on treatment outcome among

Table 2: TB treatment outcome among HIV-TB patients, N=2893

	Favorable treatment outcome				Unfavorable treatment outcome								Total
	Cured	%	Treatment Completed	%	Default	%	Failure	%	Died	%	Transferred out	%	
Total	703	24.30	1485	51.30	233	8.10	41	1.40	391	13.50	40	1.40	2893
Site of Disease													
Extra pulmonary	0	0.00	1013	80.70	89	7.10	2	0.20	134	10.70	17	1.40	1255
Pulmonary	703	42.90	472	28.80	144	8.80	39	2.40	257	15.70	23	1.40	1638
Smear status of pulmonary TB													
Smear positive	703	68.20	0	0.00	101	9.80	37	3.60	172	16.70	18	1.70	1031
Smear negative	0	0.00	472	77.80	43	7.10	2	0.30	85	14.00	5	0.80	607
History of Anti-TB Treatment													
New	545	25.60	1152	54.20	122	5.70	18	0.80	123	5.80	21	1.00	2126
Previously treated	158	20.60	333	43.40	111	14.50	23	3.00	268	34.90	19	2.50	767

Table 3: Risk factors associated with case-fatality among HIV-TB patients

Characteristic	Died	%	Alive	%	No. of patients	OR(95%CI)	p value
Total HIV-TB patients	391	13.5	2502	86.5	2893		
Sex							
Female	112	14.5	662	85.5	774	1.1 (0.9-1.4)	0.36
Male	279	13.2	1840	86.8	2119	1	
Age group							
Below 15 years	12	8.5	129	91.5	141	1	
15-64 years	374	13.8	2346	86.3	2720	1.7 (0.9-3.1)	0.07
Above 65 years	5	15.6	27	84.4	32	1.9 (0.6-6.1)	0.22
Type of TB							
Pulmonary	257	15.7	1381	84.3	1638	1.56 (1.2-1.9)	<0.001
Extra-pulmonary	134	10.7	1121	89.3	1255	1	
History of TB							
New Patients	268	12.6	1858	87.4	2126	1	0.017
Previously treated Patients	123	16.0	644	84.0	767	1.32 (1.05-1.6)	
CPT provision during TB treatment							
No	42	28.2	107	71.8	149	1	
Yes	349	12.7	2395	87.3	2744	2.7 (1.8-3.9)	<0.001
ART provision during TB treatment							
No	192	20.7	737	79.3	929	1	
Yes	199	10.1	1765	89.9	1964	2.3 (1.8-2.8)	<0.001
Both CPT & ART provision during TB treatment							
No	36	37.1	61	62.9	97	1	<0.001
Yes	193	10.1	1719	89.9	1912	5.2 (3.4-8.1)	

RNTCP = Revised National Tuberculosis Control Programme; HIV = Human immunodeficiency virus; TB = Tuberculosis; CPT = Cotrimoxazole prophylaxis therapy; ART = Antiretroviral therapy

HIV infected TB patients under program condition in Gujarat.

Treatment success rate among HIV-TB co-infected patients was found to be 75% in the present study. The treatment success rate among HIV infected TB patients was lower than among HIV non-infected TB patients reported under the programme (84%) [13].

This finding is similar to other studies in India (72%, 73% and 75%) [14-18].Treatment success rate in pulmonary TB was lower than extra-pulmonary TB (EPTB) in this study, which is also consistent with findings of two study from India indicates 89% and 83% treatment success rate among EPTB cases [14,17].

One of the important determinants of treatment success rate is death during the treatment. A high case fatality rate of 14% was reported among HIV infected TB patients in this study. Death rate among this group of patients has been reported in a range of 16%-19% in the other parts of India. [14,15,17,19,20] Studies from Ethiopia and Thailand also reported a high death rate among TB-HIV co-infected patients during TB treatment [21,22]. Case fatality in HIV-TB patients was nearly three times higher compared to HIV non-infected TB patients reported by programme during corresponding period (14% v/s 5%) [13]. In a study conducted in Kenya, the mortality was reported to be four times higher in HIV reactive as compared to HIV non-reactive TB patients during the first six months after treatment initiation [23]. Again, the death rate was higher among pulmonary TB patients as compared to EPTB patients co-infected with HIV as in case of HIV non-infected TB. Similar findings are reported from other studies [14,17].

Evidences suggest that CPT and/or ART provision during TB treatment of HIV-TB patients reduce risk of death.[10,14,16,17,23-28]In the present study, case fatality was higher among HIV/TB co-infected patients who were not provided ART during TB treatment as compared to those who were provided ART. And non-provision of ART emerged as strong risk factor for mortality. Similarly, those patients who did not receive CPT during TB treatment, case fatality was significantly high. Moreover, no provision of both ART and CPT during treatment of HIV/TB co-infected patients had significantly higher case-fatality as compared to those who received both (37% vs 10%), which indicates that increase coverage of ART and CPT decrease case fatality among HIV/TB co-infected patients.

Even in those patients who received both CPT and ART, case-fatality rate was high (10%) which was twice than HIV non-reactive TB patients reported under programme [13]. It may be possible due to late detection of HIV infection in TB patient or late initiation of ART. Findings of the study suggest that mere testing of all TB patients for HIV and provision of CPT and ART are not sufficient. Strategies beyond these interventions like early detection of HIV, intensified case finding of TB, early diagnosis of TB with more sensitive diagnostic tool and early initiation of ART and CPT during TB treatment are needed to decrease death rate among HIV/TB co-infected patients and more research is required to understand cause of high death rate among such patients.

LIMITATION

Some factors which likely to influence the case fatality like clinical manifestation, radiological presentation, drug susceptibility, other opportunistic infections and tobacco history were not ascertained in present study. Data on CD4-T cell count was not retrieved which could have added association between immune-suppression and case-fatality.

CONCLUSION

Suggested TB/HIV collaborative activities has crucial role in reducing the mortality among co-infected patients. The death rate among these patients was higher if they are not provided CPT and/or ART. Hence, the programme needs to sustain efforts of collaborative interventions to improve care for such co-infected patients. Future TB-HIV collaborative efforts should focus on early diagnosis of HIV, early diagnosis of TB using higher sensitivity diagnostics and early initiation of ART and CPT to make further impact on case-fatality.

ACKNOWLEDGMENT

We acknowledge all District Tuberculosis Offices, Senior TB-HIV and DOTS plus supervisors and Senior Treatment Supervisors for supporting evaluation.

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Date of Submission: 20/02/2014
Date of Acceptance: 19/03/2014

How to cite this article: Dave P, Kapadiya D, Modi B, Sinha L, Shah A, Vadera B. Impact of TB-HIV collaborative activities on case fatality among HIV-infected Tuberculosis patients in Gujarat, INDIA. J Res Med Den Sci 2014;2(1):1-7

Source of Support: None
Conflict of Interest: None declared