Original Article

HIV-TB Cross-referral and Collaborative Strategy: 8 Years of Our Experience from An Urban Health Centre in North India

Bhanu Mehra[1], Monika Matlani[2], Deepti Rawat[1], Hitender Gautam[3] and Preena Bhalla[1]

Department of Microbiology, Maulana Azad Medical College[1], Vardhman Mahavir Medical College and Safdarjung Hospital[2] and All India Institute of Medical Sciences[3], New Delhi, India

Abstract

Background. Human immunodeficiency virus (HIV) and tuberculosis (TB) epidemics continue to fuel each other and with dual infections with these two deadly diseases on the rise, it becomes imperative to devise effective HIV-TB collaborative strategies. The present study was designed to evaluate the existing HIV-TB cross-referral mechanism at an urban health centre; to determine HIV sero-prevalence among pulmonary TB patients referred from chest clinic to the integrated counselling and testing centre (ICTC); and to evaluate the TB suspects referred from ICTC to the chest clinic for a possible TB aetiology.

Methods. The present study was a retrospective analysis of HIV-TB cross-referrals whereby a line list of all the patients referred under this strategy from January 2006 to December 2013 was retrieved and analysed.

Results. A total of 3726 TB cases were referred to the ICTC and 641 TB suspects were identified by ICTC counsellors and referred to the chest clinic during this period. HIV sero-prevalence among TB patients was 2.8% (106 of 3726) and TB prevalence among HIV sero-positive and sero-negative TB suspects was 9.3% (10/108) and 4.3% (9/211), respectively (p=0.07). HIV prevalence was found to be significantly higher among male (n=2024) than among female (n=1702) TB patients (4.4% *versus* 0.9%; p<0.0001). Only 319 of 641 (49.8%) ICTC patients referred to the chest clinic reached there.

Conclusion. Our study highlights the strong need to scale up the integration and partnership between HIV and TB programmes for better and integrated diagnosis and care of HIV-TB co-infected patients.
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Key words: Human immunodeficiency virus (HIV), Tuberculosis (TB), Cross-referral, India, Integrated counselling and testing centre (ICTC).

Introduction

India shares the highest burden of tuberculosis (TB) in the world. According to the annual report of Revised National Tuberculosis Control Programme (RNTCP), nearly 2.2 million incident cases of TB occurred in India in the year 2012.[1] In addition, the contribution of India to the global burden of human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS) is also significant with nearly 2.39 million Indians currently harbouring the infection.[2] As the global prevalence of HIV and TB continues to increase, dual infections with these two deadly diseases are also on the rise.

Human immunodeficiency virus and TB epidemics continue to fuel and amplify each other. The devastating synergy between the two is substantiated by the fact that HIV is the greatest risk factor for the progression of latent *Mycobacterium tuberculosis* infection to active TB disease.[3,4] While the lifetime risk of developing TB in an HIV sero-negative person is around 10%, in an HIV sero-positive person co-infected with *M. tuberculosis* the figure could be as high as 50%-60%.[5] Tuberculosis is not only the first or the earliest but also the most common opportunistic infection to develop among HIV positive persons in India.[6,7] Weakening of the immune system by HIV also increases the chances of a TB re-infection, recurrence of a cured TB disease and of drug-resistant TB.[8,9] Tuberculosis, on the other hand, speeds the progression of HIV from the stage of infection to frank AIDS by enhancing viral replication, and thus, leading to a six- to seven-fold increase in viral load.[10] It is the leading cause of mortality among individuals infected by HIV.[11]

The rising rates of HIV-TB dual infections reinforce the strong and urgent need to devise effective HIV-TB collaborative strategies. Not only do the two influence and accelerate the course and progression of one another, the treatment of dual infections by different

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Correspondence and reprint requests: Dr Preena Bhalla, Director-Professor, Department of Microbiology, Maulana Azad Medical College, New Delhi-110 002, India; E-mail: preenabhalla@gmail.com

physicians under different roofs leads to fragmented patient care and duplication of resources. In addition, the HIV epidemic is adding to the number of new TB cases, the economic burden of which might soon saturate and overwhelm the capacity of the Indian health system. There is evidence that initiation of anti-retroviral treatment among HIV-TB co-infected patients on anti-TB treatment would be beneficial to the patients as it would significantly improve their CD4+ T-lymphocyte counts and reduce the mortality rates.[12,13] Keeping this in view, the RNTCP and the National AIDS Control Programme (NACP) launched a joint action plan for TB-HIV in 2001 and the TB-HIV intensified package in 2008.[14] The primary aim of this collaborative venture was to reduce TB-related mortality and morbidity among HIV infected persons and to prevent and control further spread of both the infections.

The present retrospective analysis was undertaken to evaluate the existing HIV-TB cross-referral and collaborative mechanism at an urban health centre in Delhi; to determine the presence of HIV infection in pulmonary TB patients referred from chest clinic to the integrated counselling and testing centre (ICTC); and to screen the TB suspects referred from ICTC to the chest clinic for a possible TB aetiology.

Material and Methods

The present retrospective, record-based analysis was conducted at the ICTC facility of a tertiary care health centre in Delhi. The study population comprised of all TB patients referred to the ICTC from the chest clinic of the linked hospital; as well as all those clients attending the ICTC facility, regardless of their HIV sero-status, who were identified as TB suspects and referred to the chest clinic for TB diagnosis and possible treatment.

All TB patients referred from chest clinic to the ICTC to determine their HIV status, first underwent a pre-test counselling. Following this, a written informed consent was obtained from them for HIV testing and a sero-diagnosis of HIV was made employing the algorithm as described under strategy III of the National AIDS Control Organization (NACO) guidelines.[15] Among clients attending the ICTC (excluding pregnant women), counsellors identified possible TB suspects and referred them to the chest clinic of the linked hospital on the same day as of HIV post-test counselling. A diagnosis of TB was made on the basis of sputum smear microscopy, chest radiograph and clinical profile as per the protocol defined under RNTCP guidelines.[16,17]

Monthly data of HIV-TB cross-referrals including a line list of all the patients referred under this strategy was compiled by the ICTC counsellors. The records pertaining to referrals made under the HIV-TB cross-referral strategy from January 2006 to December 2013 were retrieved and analysed in the present study. All the data was entered in a Microsoft excel sheet and analysed using the Epi Info software, Version 3.5.3, Centers for Disease Control and Prevention, Atlanta, GA, USA. Qualitative variables were expressed as numbers and percentages and the difference of proportion between them determined using the Chi-square test and Fischer's exact test. A p-value less than 0.05 was considered statistically significant.

Results

A total of 3726 confirmed TB patients referred to the ICTC from the chest clinic for HIV counselling and testing and 641 TB suspects referred from the ICTC facility to the chest clinic for TB diagnosis and possible treatment were included in the present evaluation. A total of 3726 TB cases were referred to the ICTC from the chest clinic during this eight-year period. One hundred and six (2.8%) of these cases were found to be HIV positive. Of the 3726 confirmed TB clients referred, majority, that is 3108 (83.4%) were between 15-49 years of age. Age-wise distribution of all the TB cases referred from the chest clinic to ICTC is shown in table 1. None of the TB cases under 15 years of age, 3.2% of TB cases in the 15-49 years and 1.4% in the more than 49 years age groups tested positive for HIV (p=0.9). Of these 3726 TB cases, 2024 (54.3%) were males. Gender-based description of all TB cases referred from the chest clinic to ICTC is depicted in table 2. HIV sero-positivity among males was higher compared to females (4.4% *versus* 0.9% p<0.0001).

A total of 641 TB suspects were identified by ICTC counsellors and referred to the chest clinic during this period. Of these, 264 (41.2%) were HIV sero-positive. Of the total TB suspects referred, only 319 (49.8%) reached the chest clinic. Thus, the drop-out rate among ICTC patients referred to the chest clinic was 50.2%. The drop-out rate was found to be significantly higher among HIV sero-positive (n=264) than among HIV sero-negative (n=377) TB suspects (59.1% *versus* 44% p=0.0002). A year-wise distribution of HIV negative cases referred from ICTC to the chest clinic, the number of cases reaching the chest clinic and the number of TB cases identified among them is depicted in the figure.

Nineteen of 319 (5.9%) TB suspects referred from the ICTC facility to the chest clinic and reaching there were positive for TB. The positivity rate for TB was higher (9.3%) among HIV sero-positive (n=108) as compared to a prevalence of 4.3% observed in HIV sero-negative TB (n=211) suspects (p=0.07).

An age- and gender-based description of HIV reactive TB suspects referred from ICTC to chest clinic is given in tables 3 and 4, respectively. Tuberculosis positivity among HIV sero-positive TB suspects across different age groups was as follows: could not be assessed among suspects <15 years of age (none reached chest clinic), 9.5% (9 of 95) among those 15-49 years of age and 7.7 % (1 of 13) among those older

Table 1. Age-wise description of cases referred from chest clinic to ICTC

Year	Total No. of Cases	No. of Cases <15 Years of Age (%)	No. of Cases of HIV Sero-positive	No. of Cases 15-49 Years of Age (%)	No. of Cases of HIV Sero-positive	No. of Cases >49 Years of Age (%)	No. of Cases of HIV Sero-positive
2006	67	2 (3)	0	63 (94)	2	2 (3)	0
2007	103	15 (14.6)	0	73 (70.8)	8	15 (14.6)	0
2008	198	6 (3)	0	184 (93)	12	8 (4)	1
2009	859	7 (0.8)	0	750 (87.3)	22	102 (11.9)	1
2010	811	5 (0.6)	0	730 (90)	23	76 (9.4)	2
2011	644	63 (9.8)	0	505 (78.4)	11	76 (11.8)	0
2012	554	49 (8.8)	0	441 (79.6)	9	64 (11.6)	1
2013	490	57 (11.6)	0	362 (73.9)	13	71 (14.5)	1
Total	**3726**	**204 (5.5)**	**0**	**3108 (83.4)**	**100**	**414 (11.1)**	**6**

Definitions of abbreviations: ICTC=Integrated Counselling and Testing Centre; HIV=Human immunodeficiency virus

Table 2. Gender-wise description of cases referred from chest clinic to ICTC

Year	No. of Males	No. of Males HIV Sero-positive (%)	No. of Females	No. of Females HIV Sero-positive (%)
2006	50	2(4)	17	0 (0)
2007	76	8 (10.5)	27	0 (0)
2008	132	12 (9.1)	66	1 (1.5)
2009	479	21 (4.4)	380	2 (0.5)
2010	413	22 (5.3)	398	3 (0.8)
2011	335	8 (2.4)	309	3 (0.9)
2012	280	7 (2.5)	274	3 (1.1)
2013	259	10 (3.9)	231	4 (1.7)
Total	**2024**	**90 (4.4)**	**1702**	**16 (0.9)**

Definitions of abbreviations: ICTC=Integrated Counselling and Testing Centre; HIV=Human immunodeficiency virus

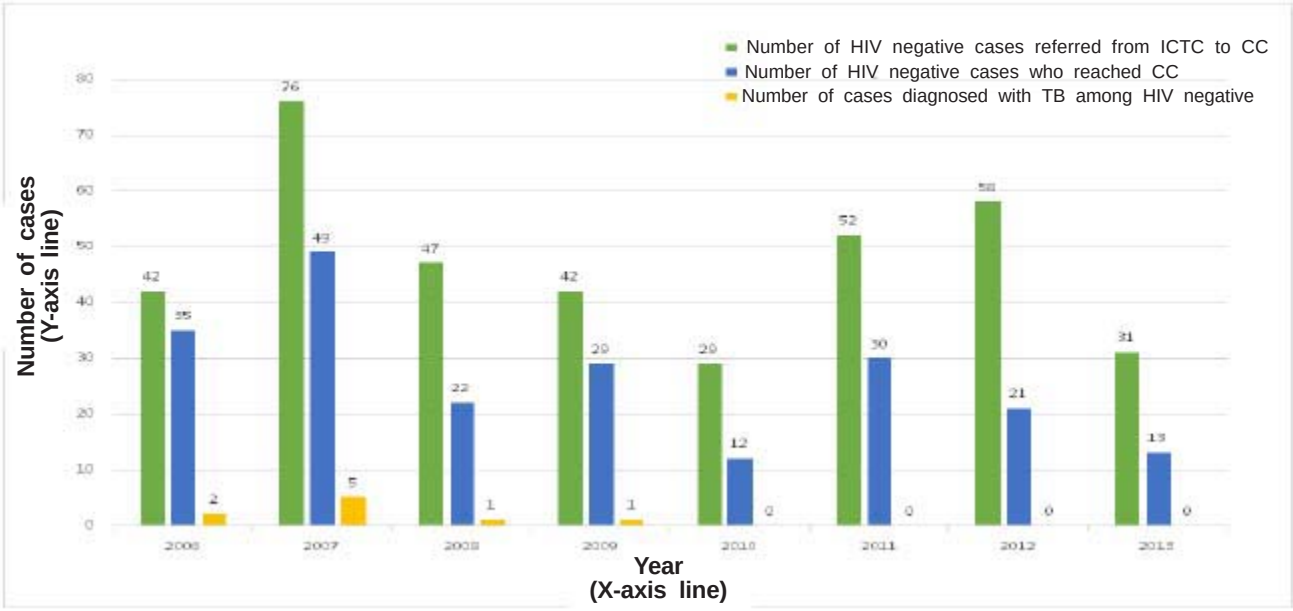

Figure. Year-wise distribution of HIV negative cases referred from ICTC to CC.
Definitions of abbreviations: CC=Chest clinic; ICTC=Integrated counselling and testing centre; HIV=Human immunodeficiency virus.

Table 3. Age-wise description of HIV* sero-positive cases referred from ICTC to chest clinic

Year	No. of HIV Sero-positive Cases Referred from ICTC to Chest Clinic (No. reached)	No. of HIV Sero-positive Cases <15 Years Referred (reached)	Number of Cases Diagnosed with TB Among HIV Sero-positive Cases <15 Years	No. of HIV Sero-positive Cases 15-49 Years Referred (No. reached)	No. of Cases Diagnosed with TB Among HIV Sero-positive Cases 15-49 Years	No. of HIV Sero-positive Cases >49 Years Referred (No. reached)	No. of Cases Diagnosed with TB Among HIV Sero-positive Cases >49 Years
2006	18 (17)	0 (0)	0	17 (16)	1	1 (1)	0
2007	30 (16)	0 (0)	0	28 (16)	2	2 (0)	0
2008	71 (19)	0 (0)	0	69 (18)	1	2 (1)	0
2009	25 (11)	0 (0)	0	24 (10)	2	1 (1)	0
2010	35 (7)	3 (0)	0	28 (3)	3	4 (4)	1
2011	64 (27)	2 (0)	0	56 (23)	0	6 (4)	0
2012	13 (5)	1 (0)	0	10 (4)	0	2 (1)	0
2013	8 (6)	0 (0)	0	6 (5)	0	2 (1)	0
Total	**264 (108)**	**6 (0)**	**0**	**238 (95)**	**9**	**20 (13)**	**1**

Definitions of abbreviations: ICTC=Integrated Counselling and Testing Centre; HIV =Human immunodeficiency virus; TB=Tuberculosis

Table 4. Gender-wise description of HIV-seropositive cases referred from ICTC to chest clinic

Year	No. of HIV Sero-positive Cases Referred from ICTC to Chest Clinic (No. reached)	No. of HIV Sero-positive Males Referred from ICTC to Chest Clinic (%)	No. of HIV Sero-positive Males who Reached Chest Clinic (%)	No. of Cases Diagnosed with TB Among HIV Sero-positive Males (%)	No. of HIV Sero-positive Females Referred from ICTC to Chest Clinic (%)	No. of HIV Sero-positive Females who Reached Chest Clinic (%)	No. of Cases Diagnosed with TB Among HIV Sero-positive Females (%)
2006	18 (17)	12 (66.7)	12 (100)	1 (8.3)	6 (33.3)	5 (83.3)	0 (0)
2007	30 (16)	23 (76.7)	12 (52.2)	2 (16.6)	7 (23.3)	4 (57.1)	0 (0)
2008	71 (19)	51 (71.8)	16 (31.4)	1 (6.3)	20 (28.2)	3 (15)	0 (0)
2009	25 (11)	18 (72)	8 (44.4)	2 (25)	7 (28)	3 (42.9)	0 (0)
2010	35 (7)	28 (80)	4 (14.3)	3 (75)	7 (20)	3 (42.9)	1 (33.3)
2011	64 (27)	48 (75)	22 (45.8)	0 (0)	16 (25)	5 (31.3)	0 (0)
2012	13 (5)	11 (84.6)	5 (45.5)	0 (0)	2 (15.4)	0 (0)	0 (0)
2013	8 (6)	5 (62.5)	5 (100)	0 (0)	3 (37.5)	1 (33.3)	0 (0)
Total	**264 (108)**	**196 (74.2)**	**84 (42.9)**	**9 (10.7)**	**68 (25.8)**	**24 (35.3)**	**1 (4.2)**

Definitions of abbreviations: ICTC=Integrated Counselling and Testing Centre; HIV =Human immunodeficiency virus; TB=Tuberculosis

than 49 years of age (p=0.11). Tuberculosis positivity was also found to be higher among HIV positive male TB suspects (9 of 84; 10.7%) in comparison to HIV-sero-positive female TB suspects (1 of 24; 4.2%) though the difference was not statistically significant (P=0.45).

Discussion

The HIV-TB collaborative venture was launched with the primary aim to promote early diagnosis and treatment of HIV in TB patients and of TB in HIV infected individuals. HIV-TB cross-referral and co-ordination is of utmost importance to improve the outcome and burden of both these infections.

Sero-prevalence of HIV in TB patients has been reported in several studies and ranges from 0.4% in 1994–1999 to 8.3% in 2003–2005 for Delhi region.[18,19] Studies from sub-Saharan Africa have reported an HIV sero-prevalence of upto 31% in TB patients.[20] In the present study, sero-prevalence of HIV in TB patients referred to ICTC was 2.8%. The variation possibly reflects the HIV sero-prevalence of the region, the time frame and duration for which the study was undertaken and the number of patients referred under the cross-referral strategy. Tuberculosis clinics have been found to form an important portal of entry for HIV diagnosis and treatment as well as to provide an opportunity for counselling, so that new infections can be prevented in the future. In addition, the higher HIV prevalence among TB patients as shown by our study as against an adult HIV prevalence of about 0.3% for Delhi region, clearly indicates that TB patients are an important population that should be screened for HIV infection.[21]

In our study, HIV sero-prevalence was highest among TB patients aged 15-49 years. High HIV sero-prevalence of 11% and 10.6% has been reported in TB patients aged 25-34 years and 35-44 years, respectively in a study conducted across 15 districts of India.[22] Another study from Mumbai[23] reported a high HIV sero-prevalence of 13.7% among TB patients aged 21-40 years. The high rate of sexual activity in this age group explains the high HIV sero-prevalence seen. A higher sero-prevalence of HIV among male than among female TB patients (8.4% *versus* 5.6%) has been reported,[22] which is in concordance with the present study. On the contrary, a higher HIV sero-prevalence among female than among male TB patients (9.4% *versus* 8.7%) has been reported in another study.[23]

In the present study, among the referrals made from ICTC to chest clinic, 5.9% of the TB suspects reaching the chest clinic were diagnosed with TB. In another study[24] conducted in Tamil Nadu, 12% of the TB suspects identified among ICTC attendees and attending the designated microscopy centres were diagnosed with TB. Tuberculosis detection rates among HIV sero-positive and sero-negative individuals were 9.3% and 4.3%, respectively. Hospital-based series from Africa have reported 40%-65% of HIV-infected patients with respiratory disease to have TB.[25,26] Significantly higher rates of TB among HIV sero-positive (55%) *versus* HIV sero-negative (25%) subjects was reported in one study,[27] while the corresponding figures were 15.9% and 23.1% among HIV sero-positive and HIV sero-negative subjects, respectively in another study.[28] ICTC initiated TB screening is now being recognised as an important tool in detecting a large burden of TB cases (both among HIV sero-positives and HIV sero-negatives). ICTC facilities are excellent sites for active TB case finding. Analysis of ICTC to RNTCP referrals from April to September, 2013 revealed that nearly 43681 diagnosed TB cases during this period came from ICTCs.[29] Moreover, keeping in view that of the 19 TB cases identified through ICTC initiated TB screening in this study, 9 (47.4%) were HIV sero-negatives; strong emphasis needs to be given to training ICTC counsellors in identifying and referring TB suspects in this category of patients as well.

In the present study, 50.2% of the referrals did not attend the chest clinic for TB diagnosis and treatment. Another study has reported a drop-out rate of 17%.[24] The high drop-out rates indicate that many patients are slipping through the detection net of this cross-referral strategy, which is a barrier to the early diagnosis and treatment of co-infected patients. While we encountered significantly higher drop-out rates among HIV sero-positive than among HIV sero-negative TB suspects (59.1% *versus* 44%), another study[24] has reported similar drop-out rates among HIV-positives and HIV sero-negatives (15% *versus* 16%). Though our study did not seek to explore the reasons for not attending RNTCP services, the significance of improving counselling services in this regard cannot be undermined. Therefore, there is a strong need to train the ICTC counsellors in TB related issues for improved and focused counselling; for designing new standard training modules / manuals and updating the existing ones for RNTCP and ICTC staff to improve the quality of referral services; to encourage regular interaction between ICTC and RNTCP personnel; to train the health-care providers about all the aspects of both the diseases; to recruit and involve outreach workers for additional counselling, support and motivation of clients through home visits; and to closely monitor the performance and impact of the HIV-TB collaborative services through regular monthly review of HIV-TB cross referral data. HIV-TB programme integration at all levels, joint planning activities between the two programmes, HIV testing and counselling for all TB patients, intensified TB case finding at ICTCs, co-location of ICTC-RNTCP services, non-governmental organisation [NGO]-government collaboration, public-private partnership, ensuring patient adherence and compliance through involvement of field workers and evolving novel communication tools focussing on HIV-TB are some of the strategies that will help to further strengthen this collateral interaction between RNTCP and NACO services and overcome the existing deficiencies.

A major strength of the present study was that it was conducted at one of the largest tertiary care centres in north India that caters to a large and diverse population base. Moreover, the sample size was large and the researchers analysed records of an 8-year long span. Therefore, the findings emerging from this study may have important implications from public health perspective.

The present study also has a few limitations. It was a single-centre based analysis the results of which cannot be generalised for or considered to be reflective of the rest of the population. Also, since this was a record-based evaluation, we could not explore the reasons for high drop-out rates among TB suspects referred from ICTC to chest clinic. Our study highlights the significant role that HIV-TB cross-referral and collateral mechanism is playing in India in detecting new HIV and TB infections as well as HIV-TB dual infections among patients referred under this strategy. Secondly, the high sero-prevalence of HIV infection among TB patients in comparison to general population clearly emphasises on the importance of implementation of routine, voluntary HIV testing for all TB patients in the country. Furthermore, the high drop-out rates among clients referred from ICTC to chest clinics require measures to improve the quality of counselling and referral services and further strengthen the synergy between RNTCP and NACO services so that better programme outcomes can be achieved in the form of improved case detection and linkage to care, better treatment outcomes, enhanced survival of patients, and better prevention and control of this deadly intersection of HIV and TB epidemics.

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