

ORIGINAL ARTICLE

A Retrospective Cohort Study of Treatment Outcome among HIV positive and HIV negative TB patients in Chandigarh, IndiaShveta Saini¹, Mukhmohit Singh², Anil Garg³^{1,2}Assistant Professor, Department of Community Medicine, Maharishi Markandeshwar Medical College and Hospital, Kumarhatti, Solan, Himachal Pradesh, India, ³State TB Officer, Government Dispensary Sector 34, Chandigarh, India.

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Abstract

Background: Tuberculosis (TB) and the HIV epidemics have been well known previously but now these are emerging as a combined epidemic to pose new public health challenges. TB is the most common opportunistic infection found among HIV positive individuals. **Aims & Objective:** To find the prevalence of HIV infection among the TB patients diagnosed and put on treatment under RNTCP. 2. To assess their treatment outcomes in Chandigarh. **Material & Methods:** The present study was designed as a retrospective cohort study among the adult population (>18 years) in Chandigarh from April 2012 - March 2014. All the TB patients registered for treatment at the 17 DMCs of Chandigarh, during this period were taken as the study population. The treatment outcome among TB-HIV co-infected patients was compared with those having only Tuberculosis. **Results:** From 1st April 2012 - 31st March 2013, a total of 3,551 patients were registered under RNTCP for treatment of tuberculosis. Among the total patients put on DOTS (3,551), 63.2% (2,246) were males and 36.7% (1,305) were females. A total of 3,516 TB patients had their blood tested for HIV. Out of these patients, 88 (2.47%) were tested positive for HIV. HIV positive status was also found to be significantly associated with occurrence of extra pulmonary tuberculosis ($\chi^2= 17.42$; df 2; p 0.0001). Category – II treatment was found to be slightly more among the HIV positive TB patients as compared to the HIV negative patients. From the total sample, 2.19% (78) patients were later diagnosed as having drug resistant tuberculosis with only one (01) patient being co-infected with HIV. Out of all the TB-HIV co-infected patients, 29.55% were declared cured at the end of the treatment. A total of 63.64% of co-infected patients had completed their treatment. Death as an outcome was significantly associated with HIV positive status (1.14%) as compared to HIV negative patients. **Conclusion:** Integration of TB-HIV collaborative activities at every level will strengthen our battle to control TB and HIV globally.

Keywords

TB; HIV; Co-infection; RNTCP; Outcome; Cure; Treatment; Died

Introduction

Tuberculosis (TB) and the HIV epidemics have been well known previously but now these are emerging as a combined epidemic to pose new public health challenges.(1) HIV positive patients have a higher

propensity to acquire secondary tuberculosis following a primary infection.

HIV infection provides a suitable environment for promotion of secondary TB infection both in people with recently acquired TB infection and with latent M. Tuberculosis infection. As per the database for

global tuberculosis report 2014, approximately 120,000 HIV-positive TB cases occurred in India in 2013.(2) India has the highest TB burden in the world and accounts for 23% of the global incidence of TB cases.(3)

Early diagnosis and effective treatment of active TB disease in HIV-infected patients is imperative for curing TB and reducing its ill effects on progression of HIV. High-quality diagnosis and treatment for TB is provided nationwide under the Revised National TB Control Programme (RNTCP). The standardized supervised regimens of RNTCP are equally effective in HIV-positive patients.(4) The interaction between HIV and TB is bidirectional and synergistic. On one hand, HIV infection predisposes to the development of active TB, and, on the other, the course of HIV-related immunodeficiency is worsened by active TB infection leading to a high case fatality rate.(5)

As per NACO India HIV estimations report of 2015(6), the prevalence of HIV infection in adult population has been estimated to be 0.26% of the population. Although country has showed a steady decline in HIV prevalence with 0.34% in 2007 to 0.26% in 2015, Chandigarh along with Maharashtra, Tripura and Tamil Nadu has shown estimated adult HIV prevalence greater than the national prevalence (0.26%). TB continues to be a public health challenge in India and is estimated that 1.9 million new cases of TB occur in India annually.

India has well-structured and functional national programs for the control of both HIV and TB; the National AIDS Control Program (NACP) and the Revised National TB Control Program (RNTCP) respectively. TB/HIV collaborative activities had started in 2001 and now with development of intensified TB/HIV comprehensive package of services being offered to all states in the country since 2011.(7)

Also, it is noteworthy that TB is the most common opportunistic infection (OI) among HIV positive patients and about a third of HIV infected individuals worldwide are co-infected with TB infection. To achieve optimal results and effectiveness of the TB/HIV co-ordination activities, the HIV care providers do screen their patients for TB in the initial phase of therapy and accordingly establish linkages with RNTCP for further evaluation.(8)

Aims & Objectives

1. To find the prevalence of HIV infection among the TB patients diagnosed and put on treatment under RNTCP.
2. To know the percentage of referral of TB patients to the nearest ICTC for HIV counseling and testing in Chandigarh.
3. To compare the outcomes of TB treatment in TB/HIV co-infected patients and only TB patients registered under the RNTCP within the same area.

Material & Methods

As per details from Census 2011(9), Chandigarh has a population of 10.55 Lakhs. Chandigarh has Punjab, Haryana and Himachal Pradesh in its neighborhood. Hence there is a continuous influx of migratory population in the city.

The present study was designed as a retrospective cohort study among the adult population (>18 years) in Chandigarh from April 2012 - March 2014. All the TB patients registered for treatment at the 17 DMCs of Chandigarh (3,551), during this period were taken as the study population. These also included the patients who were referred from the ART centre (37) for initiation of TB treatment. They were followed up till their treatment outcome was known. The treatment outcome among TB-HIV co-infected patients was compared with those having only Tuberculosis.

Inclusion Criteria:

- Adults 18 years of age or more.
- Residents of Chandigarh.
- Category I or Category II patients as per RNTCP.
- All HIV positive patients diagnosed for TB and referred from ART Centre.
- All the patients who had started their anti-tubercular treatment in the year 2012 and 2013 and their treatment outcome declared in 2013-14.

Exclusion Criteria:

- Patients not residing in Chandigarh.
- Patients not registered in RNTCP.
- Patients already undergoing treatment for Drug Resistant Tuberculosis.
- Age <18 years.

Study Population and Strategy:

There are a total of 17 DMCs in Chandigarh. In the year 2012 and 2013, 3,551 new TB Cases including both Pulmonary and Extra pulmonary, were enrolled

at the Designated Microscopy Centers (DMC). The data of all the eligible patients enrolled during the above said period was taken from the DMCs with due permission of Director Health Services, Chandigarh. The data of these patients was analyzed in terms of: socio-demographic details, category of tuberculosis as per RNTCP - category I or category II: categorization of the patients was done by the medical officer in-charge of the DMC, type of tuberculosis - pulmonary or extra pulmonary, HIV status, treatment outcome as per RNTCP - Cured, Treatment complete, Loss to follow up, Treatment Failure, change of regimen, Not evaluated or died.

Diagnosis of Tuberculosis in Chest Symptomatics:

The diagnosis of tuberculosis was based on the RNTCP protocol. TB was suspected in a patient if he/she had any of the following four cardinal symptoms: Cough more than 2 weeks with/without expectoration, Loss of weight, Loss of appetite, Evening rise of fever with night sweats, Ziehl-Neilsen (ZN) staining of sputum for demonstration of acid-fast bacilli (AFB) was then performed by experienced lab technician as per RNTCP recommendations at the DMC. Patient was then categorized accordingly and put on treatment by the concerned medical officer of the DMC.

Diagnosis of HIV positive state in Tuberculosis patients:

All the patients put on Anti-tubercular Treatment (ATT) were referred to the nearest Integrated Counseling and Testing Center (ICTC) for provider initiated counseling and HIV testing. Any patient tested and confirmed positive for HIV at the ICTC was first put on ATT and then referred to the ART center at PGIMER, Chandigarh for receiving ART. As per the recent guidelines of WHO, all the TB-HIV co-infected patients were put on ART irrespective of the CD4 count. All the co-infected patients were also given CPT at the ART center.

Diagnosis of Tuberculosis in HIV positive patients:

The World Health Organization currently recommends (10) that all HIV infected persons should be screened for TB, and HIV infected persons without active TB disease be evaluated for latent TB infection. The WHO recommends TB screening at the time that HIV infection is diagnosed, before the initiation of antiretroviral therapy and at regular intervals during follow up. All the patients diagnosed as HIV positive were screened for tuberculosis at the ART Center, PGIMER, Chandigarh. Screening was done through clinical assessment and radiological methods. Any patient reported as tuberculosis

suspect (pulmonary or extra pulmonary) was then referred to the nearest DMC for sputum microscopy and further initiation of ATT.

Treatment Outcome: Treatment outcomes used in the study were as per WHO definitions for tuberculosis (11) as follows:

- Cured: Initially sputum smear positive patient who has completed treatment and had negative sputum smears on two occasions, one of which is at the end of the treatment is declared as cured.
- Treatment completed: Initially sputum smear negative patient who has received full course of treatment and has not become smear positive at the end of the treatment;
Or
Extra pulmonary TB patient who has received full course of treatment and has not become smear positive during or at the end of treatment is also declared as treatment completed.
- Treatment Success: The sum of cured and treatment completed.
- Treatment Failed: Any TB patient who is smear positive at five months or more after starting the treatment is considered as 'Treatment Failed'.
- Lost to Follow up: A TB Patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.
- Died: Patient who died during the course of treatment regardless of cause is declared as 'Died'.

Ethical Approval: Ethical approval to conduct the study was sought from the ethical committee of State Health Society, Chandigarh, vide letter number NRHM/Chd/12/205.

Data Analysis: The data was analyzed using Microsoft excel and SPSS software version 21.

Results

A total of 3551 patients were registered under RNTCP for treatment of tuberculosis during the study period. Out of these patients, 37 diagnosed TB patients were referred from the ART center at PGIMER, Chandigarh for initiation of TB treatment. Among the total patients put on DOTS (3,551), 63.2% (2,246) were males.

Majority of TB cases, 1,340 (37%) occurred in the age group of 29 - 39 years having maximum number of infected males 883 (65.9%) than in any other age group. In age group 18 - 28 years, 48.3% females were infected as compared to 34.1% in 29 - 39 years

age group. Thereafter, it was seen that as the age advanced, the number of TB patients decreased ([Figure 1](#)).

Although all the TB patients were referred to ICTC for counselling and HIV testing, however there were 35 (0.98%) such TB patients who did not get their HIV status tested probably because of the social taboo associated with HIV. A total of 3,516 (99.02%) TB patients had their blood tested for HIV. Out of these patients, 88 (2.47%) were tested positive for HIV ([Table 1](#)). Among the 88 HIV positive individuals, 37 patients were referred from ART centre and were diagnosed as having tuberculosis at the DMC situated at PGIMER, Chandigarh. All of these patients were subsequently initiated on ART and DOTS.

On analyzing the data, HIV positive status was found to be significantly associated with occurrence of extra pulmonary tuberculosis ($\chi^2= 17.42$; df 2; p 0.0001). Out of 88 TB-HIV co-infected patients, 57.95% had extra pulmonary type of tuberculosis as compared to 36.49% extra pulmonary tuberculosis among the HIV negative patients. Majority of the HIV negative TB patients (63.51%) were found to have pulmonary tuberculosis (63.51%). ([Table 2](#))

[Table 3](#) shows that among all the HIV positive patients, category - I of anti-tubercular treatment was seen in 76.14% patients. Category - II treatment was found to be slightly more among the HIV positive TB patients as compared to the HIV negative patients. However, the results were not statistically significant showing no association of previous TB exposure and reoccurrence of TB infection among the HIV positive patients.

Out of all the TB-HIV co-infected patients, 29.55% were declared cured at the end of the treatment. A total of 63.64% of co-infected patients had completed their treatment as compared to 47.32% among the patients infected with tuberculosis only. On statistical analysis, the result was found to be highly significant with a p value <0.0001. None of the co-infected patients defaulted from the treatment whereas loss to follow up rate was 2.19% among the HIV negative patients and 2.86% among the patients with unknown HIV status. Treatment Failure rate was seen to be highest among the patient with unknown HIV status (11.43%) followed by 4.55% in the HIV-TB co-infected patients. From the total sample, 2.19% (78) patients were later diagnosed as having Drug resistant tuberculosis with only one (01) patient being co-infected with HIV. However, switching over

to category - IV (Drug Resistant Tuberculosis) was seen to be significantly associated with positive HIV status ($\gamma^2: 225$; df=2; p value <0.0001). Death as an outcome was significantly associated with HIV positive status (1.14%) as compared to HIV negative patients (0.88%) ([Table 4](#)).

Discussion

TB is the most common life-threatening opportunistic infection in patients with HIV/AIDS in developing countries. In this study, it was found out that 99% of the patients knew their HIV status. Only a fraction of patients did not get their HIV status tested at any of the ICTC in the city. This shows an effective referral mechanism between RNTCP and National AIDS Control Organization (NACO), Chandigarh. All the chest symptomatic patients coming to the 17 DMCs were appropriately categorized and put on ATT by the concerned medical officer. Prevalence of co-infection among the TB patients was found to be 2.47% as opposed to 20.5% reported by Oshi *et al* (12) in Nigeria in 2014. No significant association was found among the occurrence of co-infection and retreatment cases. However, extra-pulmonary TB was found to occur in higher frequency among the HIV positive patients, similar findings were also reported by Sharma *et al* (13) in northern India. This is in contrast to the findings reported by Shastri *et al* (19) in Karnataka where they reported pulmonary involvement in about 70% of patients. This could be because of lack of reporting or diagnosis of extra pulmonary tuberculosis among the HIV positive individuals. TB being most common opportunistic infection among the HIV positive individuals puts them at a greater risk of being advanced immune-suppressant. Better and quick diagnostic techniques are required for the diagnosis of TB among the HIV positive individuals in order to reduce the mortality associated with co-infection state.

More than 80% of TB-HIV co-infected patients had successfully completed their treatment and were cured of tuberculosis. Similar findings were reported by Sharma *et al* (15) in northern India.

Dedication and commitment of co-infected patients and the associated staff members of DMC and ART center in getting the TB treatment completed was seen as there was absolutely no default of treatment reported among the TB-HIV co-infected patients. This result was found to be in concordance with the findings reported by Shastri *et al* (14) in Karnataka.

Treatment default was found to be higher among the TB patients with unknown HIV status, probably due to their careless attitude towards their disease.

Death rate was contrastingly found to be higher among the HIV positive patients. Similar results were also published by WHO (15) in 2014 showing a case fatality rate of about 13% among the TB-HIV co-infected patients.

Conclusion

Co-infected patients showed better TB treatment success rates with no default in the treatment. Treatment failure rate was more among the co-infected patients may be owing to their immune-compromised state. Death rate among the co-infected patients was considerably higher among the TB-HIV co-infected patients. Integration of TB-HIV collaborative activities at every level will strengthen our battle to control TB and HIV globally. There is an urgent need to strengthen our efforts of ACSM (Advocacy, Communication and Social Mobilization) to motivate the patients for testing of their HIV status and hence, to reduce the morbidity and mortality associated with co-infection.

Recommendation

TB-HIV co-infection epidemic is a public health problem which can be zeroed down with effective linkage between RNTCP and NACP. Prompt diagnosis and treatment of active TB patients will help in bringing down the morbidity and mortality associated with TB-HIV co-infection.

Limitation of the study

Excluding the patients taking anti-tubercular treatment from the private sources and not registered under RNTCP as only co-infected patients taking treatment under RNTCP in Chandigarh have been included in the study.

Another limitation is non-availability of information regarding the sites of involvement in the extra pulmonary tuberculosis. Treatment completion rates depend a lot on the site of extra pulmonary infection.

Relevance of the study

The present study provides an estimate for the prevalence of TB/HIV co-infection in Chandigarh. The study also adds to the current knowledge of treatment outcomes among the TB/HIV co-infected patients.

Authors Contribution

SS: Principle investigator, data collection and write up; MS: Data Analysis, interpretation and discussion; AG: Logistic support, data collection and proof reading. All the authors actively participated in editing and final proof reading of the paper.

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Tables

TABLE 1 PREVALENCE OF HIV INFECTION AMONG TB PATIENTS

	Frequency	Percent
HIV +	88	2.47
HIV-	3428	96.53
Unknown	35	0.98
Total	3551	100

TABLE 2 ASSOCIATION OF HIV STATUS AND TYPE OF TUBERCULOSIS (N=3516)

	Type of Tuberculosis		
	Pulmonary	Extra pulmonary	Total
HIV +	37 (42.05%)	51 (57.95%)	88 (100%)
HIV -	2177 (63.51%)	1251 (36.49%)	3428 (100%)
Total	2214	1302	3516

$\chi^2 = 17.42$; $df 2$; $p 0.0001$ *A total of 35 patients with unknown HIV status have been excluded from the analysis

TABLE 3 CATEGORY OF TREATMENT AMONG TUBERCULOSIS PATIENTS

HIV Status	Treatment category		Total
	Category I	Category II	
HIV +	67 (76.14%)	21 (23.86%)	88
HIV -	2688 (78.41%)	740 (21.59%)	3428
Unknown	26 (74.29%)	9 (25.71%)	35
Total	2781 (78.32%)	770 (21.68%)	3551

TABLE 4 TREATMENT OUTCOME AMONG HIV POSITIVE AND HIV NEGATIVE TB PATIENTS (N=3,551)

Outcome	HIV Positive	HIV negative	Unknown	χ^2	p value
Cured	26(29.55%)	1522(44.40%)	15(42.86%)	0.432E+04; df 2	<0.0001
Treatment complete	56(63.64%)	1622(47.32%)	14(40%)	0.448E+04; df2	<0.0001
Loss to Follow up	0	75(2.19%)	4(11.43%)	219; df2	<0.0001
Treatment Failure	4(4.55%)	102(2.98%)	2 (4.86%)	266; df2	<0.0001
Treatment regimen changed to cat IV	1(1.14%)	77(2.25%)	0	225; df2	<0.0001
Died	1(1.14%)	30(0.88%)	1(2.86%)	78.8; df2	<0.0001
Total	88(2.47%)	3428(96.54%)	35(0.99%)	-	-

Figures

FIGURE 1 AGE AND SEX WISE DISTRIBUTION OF TB PATIENTS

