



Provider-initiated HIV testing & counselling in incident tuberculosis cases under National TB Programme conditions at a tertiary care teaching hospital in Tirupati, south India

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Background & objectives: As sparse published data are available regarding burden of human immunodeficiency virus (HIV) infection in incident tuberculosis (TB) cases at tertiary care teaching hospitals under National TB Programme conditions from India, the present study was designed to assess the proportion of referred registered TB patients who had actually undergone HIV testing and HIV-seropositivity in these.

Methods: This was a study of provider-initiated HIV testing and counselling in patients registered for the treatment under Revised National TB Control Programme (RNTCP) of Government of India at a tertiary care teaching hospital in Tirupati, south India, during 2012-2013.

Results: Between January 2012 and June 2013, 610 adult patients registered under RNTCP who were referred to Integrated Counselling and Testing Centre for HIV testing, were prospectively studied. Of these, 458 patients (75%) [mean age: 38.6±16.3 yr; 295 (64.4%) males] underwent HIV testing; HIV-co-infection was present in 21 (4.6%) patients. A significantly higher proportion of HIV co-infection was evident in PTB compared with EPTB [13/179 (7.2%) vs 8/279 (2.8%); respectively, $P=0.038$] and in previously treated patients compared to new patients [6/51 (11.8%) vs 15/407 (3.7%); respectively, $P=0.009$].

Interpretation & conclusions: The findings of this study showed that a higher proportion of TB patients underwent HIV testing (75%) compared to the national figure of 63 per cent in 2013-2014. HIV seropositivity (4.6%) in TB patients who underwent HIV testing was similar to the five per cent figure observed at national level during 2013-2014. The HIV status of 25 per cent of patients with incident TB still remained unknown, suggesting a need for better integration and co-ordination for effective management of HIV-TB co-infection.

Key words HIV infection - provider-initiated HIV testing and counselling - tuberculosis

Tuberculosis (TB) is a major public health problem world over. Following the introduction of effective anti-TB treatment in the mid-1940s, cure of TB became a reality. However, the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) pandemic in the early 1980s has resulted in a global resurgence of TB¹. Worldwide, in 2014, 3.2 million notified TB patients (51% of the notified TB cases) knew their HIV status. In 2014, there were an estimated 9.6 million new cases of TB, of whom, 1.2 million (12%) were co-infected with HIV, and 0.4 million (26.7%) of the 1.5 million people who died from TB were HIV positive². TB is the most common opportunistic infection among people living with HIV (PLWHIV). In 2014, HIV-associated TB accounted for 25 per cent of all TB deaths and one-third of the estimated 1.2 million deaths from HIV/AIDS².

Recognizing the importance of the deadly interaction between TB and HIV, the National (policy) Framework for Joint TB/HIV Collaborative Activities was jointly developed by the Revised National TB Control Programme (RNTCP) and the National AIDS Control Programme (NACP)³⁻⁷. Presently, all TB patients diagnosed at Designated Microscopy Centres (DMC) are referred to the Integrated Counselling and Testing Centres (ICTC) for HIV testing, PLWHIV are screened for symptoms of TB and those with suggestive symptoms of TB are referred to the RNTCP diagnostic and treatment facility located in the same institution for TB diagnosis⁷.

At a national level, about three per cent of TB patients registered under RNTCP are co-infected with HIV³. According to the 13th round of HIV Sentinel Surveillance implemented during 2012-2013 in 34 States and Union Territories in the country, the highest HIV prevalence among antenatal clinic attendees (considered proxy for prevalence among general population) was recorded in small States such as Nagaland (0.88%), Mizoram (0.68%), Manipur (0.64%); followed by large States such as undivided Andhra Pradesh (0.59%) and Karnataka (0.53%)⁵. In high-prevalent States and districts, HIV seropositivity among TB patients was over 10 per cent and was observed to be as high as 40 per cent in certain districts^{5,7}.

In spite of over a decade of unique involvement of medical colleges in the RNTCP⁸, no data are available on the performance of the referral mechanism 'under Programme conditions' at a medical college in India.

Recognizing the public health importance of detecting HIV infection among TB patients presenting the healthcare facility, the present study was designed to prospectively study the following under Programme conditions at a medical college tertiary care teaching hospital in Tirupati, south India: (i) to assess the proportion of TB patients registered under RNTCP who were referred for testing and had actually undergone HIV testing; and (ii) among the TB patients who were actually tested for HIV, to assess the proportion of patients who had tested HIV seropositive.

Material & Methods

The study was conducted at the Sri Venkateswara Institute of Medical Sciences (SVIMS), Tirupati, Andhra Pradesh, between January 2012 and June 2013. The study protocol was approved by the institutional ethics committee and informed written consent was obtained from all patients.

For assessing the proportion of TB patients registered under RNTCP who were referred for HIV testing and had actually undergone testing, sample size was calculated as follows. The proportion of TB patients who have actually undergone HIV testing in the field setting at the national level was 65 per cent^{4,5}. Considering this proportion as 80 per cent with a precision of five per cent and a desired CI of 95 per cent, 246 patients were required. For assessing the proportion of patients who tested HIV positive among those who had actually undergone HIV testing, the sample size was calculated as follows. The proportion of TB patients who have tested HIV seropositive among those who have actually undergone HIV testing in the field setting at the national level was six per cent^{4,5}. Considering this proportion as 11 per cent, with a precision of 2.5 per cent and a desired CI of 95 per cent, the sample size required was calculated to be 553. Sample size calculations were done using nMaster[®] software (Version 2) [Copyright[©] Department of Biostatistics, Christian Medical College (CMC), Vellore; kind courtesy: Dr L. Jeyaseelan, Professor, Department of Biostatistics, CMC, Vellore].

All incident 'new' as well as 'retreatment cases' diagnosed to have and treated for various forms of TB between January 2012 and June 2013, who were unaware of their HIV status, were studied. As per the National Framework for Joint HIV/TB Collaborative Activities of the Central TB Division and National AIDS Control Organization (NACO), Government of India norms⁷, all patients diagnosed to have TB were given referral for voluntary counselling and HIV testing at the ICTC.

In all patients, a detailed history was obtained and a thorough physical examination was carried out. The method of confirmation of diagnosis of TB was recorded. As per the guidelines^{7,9}, patients not willing for HIV testing or sharing their HIV test result were not forced to take the test or disclose this information. In the ICTC setting, rapid HIV tests were used for HIV testing as per NACO recommendations⁹. Three rapid test kits that detect >99.5 per cent of all HIV-infected patients with a false-positive results of <2 per cent as per the NACO guidelines⁹ were used. The first test had the highest sensitivity and the second and third tests had the highest specificity. If the result of the first test (A1) (COMBAIDS[®] - RS Advantage-ST HIV 1+2 Immunodot Test Kit; Span Diagnostics, Sachin, India) was negative, then the person was declared as HIV negative. When the result of the first test was positive, then the same blood was tested by two additional tests [A2 (PAREEKSHAK[®] HIV-1/2 Triline Card Test; Bhat Bio-Tech, India (P) Ltd., Bengaluru, India) and A3 (AIDSCAN[®] HIV-1/2 Trispot Test kit; Bhat Bio-Tech, India (P) Ltd., Bengaluru, India)] using different kits. If all the three tests yielded positive results, the sample was considered positive. However, if the first test (A1) was positive and the second test (A2) was negative, a third test (A3) was used to confirm the result. If the result of the third test (A3) was positive, the sample was considered as indeterminate and such patients were advised to undergo repeat testing after 2 to 4 wk. If the first test (A1) was positive and the second (A2) and third test (A3) results were negative, the sample was considered as HIV negative.

TB was treated in all the patients as per the RNTCP norms⁴. Patients who tested positive for HIV were referred to the ART Centre at Sri Venkateswara Ramnarain Ruia Government General Hospital, Tirupati, for further workup and management as per NACO guidelines⁹.

Statistical analysis: Data were recorded on a predesigned proforma and managed using Excel 2007 (Microsoft Corporation, Redmond, WA, USA). Descriptive statistics were performed by computing the frequencies (percentage) in each category. For the quantitative variables, approximate normality of the distribution was assessed. Variables following normal distribution were summarized by mean and standard deviation. Other variables were summarized as median (interquartile range). HIV seropositivity across various age groups, between genders, treatment categories and site of TB was compared using Chi-square test.

Statistical software package IBM SPSS Statistics 20 (IBM Corporation, Chicago, IL, USA) was used for statistical analysis.

Results

During January 2012 to June 2013, 560 patients were diagnosed to have various forms of TB and were registered for treatment at the DOT Centre, SVIMS, Tirupati. Of these, 12 (2.2%) were initial defaulters and could not be traced; 14 patients were known to have HIV infection and were on treatment. The remaining 534 patients together with 76 patients who were diagnosed to have TB elsewhere and were referred to DOT centre at SVIMS for treatment (n=610) were included in the study. Their mean age was 39.8±16.6 (range: 6 to 88 yr) yr; 320 (52.5%) were under 40 yr of age. Men outnumbered women (M:F=1.8:1). Extrapulmonary TB (n=371; 61%) was more frequently seen than pulmonary TB (n=239; 39%). A majority of TB patients (n=539; 88.4%) were new patients. Seventy one patients (11.6%) were previously treated patients; this included treatment after default (n=27), relapse (n=12), treatment failure (n=2) and others (n=30). In patients with extrapulmonary TB, pleural TB (23.6%), lymph node TB (21.5%) and neurological TB (21.3%) were the most common sites of involvement.

Of the 610 patients, HIV test results were available for 458 patients (75%). Their mean age was 38.6±16.3 yr (range: 6-88 yr). Majority of them (n=295; 64.4%) were males. In the present study, 21/458 (4.6%) patients, with incident TB for whom test results were available, tested HIV seropositive. The mean age of HIV seropositive patients (n=21) was 38.2±7.1 (range: 25-55 yr) yr. Majority of them (n=13) were males. Most of the patients (n=13) had pulmonary TB.

Presence of HIV infection in incident TB cases across age ranges is shown in Table I. A significant number of HIV seropositive patients were in the 31-40 yr age group ($P=0.002$). Comparison of HIV seropositivity in patients with pulmonary and extrapulmonary TB for whom HIV test results were available is shown in Table II. HIV seropositivity was significantly higher in patients with pulmonary TB compared to those with extrapulmonary TB ($P=0.038$). Comparison of HIV seropositivity between 'new' and 'previously treated' patients is shown in Table III. HIV positivity was significantly higher in previously treated patients compared to new cases ($P=0.009$). There was

Table I. Presence of HIV infection in incident TB cases across various age groups

| HIV status | Age (yr) | | | | | | P |
|------------|------------|--------------|--------------|--------------|--------------|------------|-------|
| | <20 (n=71) | 21-30 (n=98) | 31-40 (n=88) | 41-50 (n=86) | 51-60 (n=66) | >60 (n=49) | |
| Negative | 71 | 95 | 77 | 81 | 64 | 49 | 0.002 |
| Positive | 0 | 3 | 11 | 5 | 2 | 0 | |

Table II. Comparison of HIV seropositivity in patients with pulmonary and extrapulmonary tuberculosis for whom HIV test results were available (n=458)

| Type of TB | HIV positive (%) | HIV negative | Total | P |
|----------------|------------------|--------------|-------|-------|
| Pulmonary | 13 (7.2) | 166 | 179 | 0.038 |
| Extrapulmonary | 8 (2.8) | 271 | 279 | |

Table III. Comparison of HIV seropositivity between 'new' and 'previously treated' patients for whom HIV test results were available (n=458)

| Treatment category | HIV positive (%) | HIV negative | Total | P |
|-----------------------------|------------------|--------------|-------|-------|
| New patients | 15 (3.7) | 392 | 407 | 0.009 |
| Previously treated patients | 6 (11.8) | 45 | 51 | |

no significant difference in the HIV seropositivity between male and female genders (4.9 vs 4.4%, respectively, $P=0.806$).

Comparison of HIV seropositivity in incident TB cases documented in published studies from India from 2000 onwards and the present study is shown in Table IV.

Table IV. Comparison of HIV seropositivity in diagnosed adult TB patients in published studies from India during the last decade (2005-2015)

| Variable | Hussain <i>et al</i> ¹⁰ | Piramanayagam <i>et al</i> ¹¹ | Bahl <i>et al</i> ¹² | Sawant <i>et al</i> ¹³ | Kaur <i>et al</i> ¹⁴ | Manjareeka and Nanda ¹⁵ | Present study |
|------------------------|--|--|--|--------------------------------------|---|--|-----------------|
| Study setting | TB Demonstration, Research & Training Centre, Agra | AIIMS, New Delhi | Chest Diseases Hospital of Government Medical College, Jammu | BYL Nair Charitable Hospital, Mumbai | SGRDIMSR Rural Tertiary Care Hospital, Amritsar | Central Hospital of South Eastern Railway, Kolkata | SVIMS, Tirupati |
| Study period | 2001-2004 | 2003-2005 | 2003-2004 | One year* | 2010-2011 | 2000-2012 | 2012-2013 |
| Number studied | 600 | 374 | 5387 | 420 | 618 | 406 | 610 |
| HIV seropositivity (%) | 4.3 | 8.3 | 1.6 | 9 | 1.2 | 12.3 | 4.6 |

*Year not specified. TB, tuberculosis; AIIMS, All India Institute of Medical Sciences; BYL Nair, Bai Yamunabai Laxman Nair; SGRDIMSR, Sri Guru Ram Das Institute of Medical Sciences and Research; SVIMS, Sri Venkateswara Institute of Medical Sciences

Discussion

HIV testing of TB patients is now routine through provider-initiated HIV testing and counselling (PITC) and has been implemented in all States with the intensified TB-HIV package³. Information regarding the HIV status of a person also has the advantage of providing an opportunity to administer prophylaxis for opportunistic infections and thereby reducing morbidity and mortality. Furthermore, the spouse and relatives of HIV-seropositive patients may also benefit from counselling regarding HIV infection, its modes of transmission and prognosis, preventing the spread of infection.

In immunocompetent individuals, pulmonary TB is the most common form observed in 85 per cent of patients while extrapulmonary TB is seen in 15 per cent^{1,16,17}. In the present study, patients with extrapulmonary TB outnumbered those with pulmonary TB (61 vs 39%, respectively). This could be due to referral bias as patients with clinically evident extrapulmonary TB and those with obscure disease are referred to teaching hospitals attached to medical colleges for invasive diagnostic testing.

In the present study, HIV status was known for 458 of the 610 patients (75%) referred to the ICTC for testing. In comparison, worldwide, the proportion

of notified TB cases in 2014 with a documented HIV test result was 51 per cent. In India, HIV status was known in 63 per cent patients of TB registered during the period 2013^{4,5}. Observations from the present study indicated that HIV status was known in a higher proportion of TB patients compared to the global (51%) and the national (63%)^{4,5} figures.

Further, 21 of the 458 patients (4.6%) for whom HIV test results were available were found to be HIV seropositive. Given that Andhra Pradesh is a high HIV burden State⁵, the figure of 4.6 per cent appears to be a relatively low figure that is closer to the national figure of 5 per cent⁶. Comparison of HIV seropositivity in diagnosed TB patients in published studies¹¹⁻¹⁵ from India showed a wide variation ranging from 1.2 to 12.3 per cent. However, unlike the present study, none of these studies¹¹⁻¹⁵ were carried out under Programme conditions in a medical college setting. There is a need for conducting community-based studies with a large sample size to study the reasons for these variations.

In a study from Chennai¹⁸, 20 (83.3%) of the 24 HIV-seropositive patients were less than or equal to 40 yr of age. Similarly, in a study from Pune¹⁹, most of the HIV-seropositive incident TB cases were in the age group of 21-40 yr. Further, in a study from Delhi²⁰, there was an increase in seroprevalance of HIV with rising age: prevalence was 0.51 per cent in 15-24 yr group, 1.55 per cent in 25-34 yr group and 1.66 per cent in the 35 yr and more group. Observations from the present study and other studies (Table IV)¹⁰⁻¹⁵ indicated that majority of patients with HIV-TB co-infection were in the 31-50 yr age group who were in their economically most productive years. Our study suggested that both genders were equally susceptible to HIV infection.

HIV seropositivity was found to be significantly higher in patients with pulmonary TB compared to those with extrapulmonary TB. In patients with HIV/AIDS, unlike other opportunistic infections which occur at CD4+ counts below 200/ μ l, active TB can manifest throughout the course of HIV disease²¹. Clinical presentation of TB in HIV-infected individuals depends on the level of immunosuppression due to HIV infection. In patients with relatively intact immune function (CD4+ T-lymphocyte count >200/ μ l), pulmonary TB is more frequently seen than extrapulmonary TB^{22,23}. Even though CD4+ T-lymphocyte counts were not recorded in the HIV-seropositive patients in the present study, the fact that majority of these patients manifested pulmonary TB suggested that probably the immune

function in these patients was relatively intact and they had early HIV infection.

In the present study, HIV infection was significantly higher in previously treated patients compared to new cases. As previously treated patients are more likely to harbour drug-resistant TB, co-infection with HIV renders their treatment to be a therapeutic challenge. Given the limited number of certified laboratories and paucity of facilities for the management of drug-resistant TB under Programme conditions, increased HIV seroprevalence in previously treated TB cases appears to be a major challenge for TB control.

Globally, in 2014, the proportion of notified TB cases with a documented HIV test result (51%) showed an increase of more than 15 times over the figure of 3.1 per cent observed in the year 2004². In India, the proportion of TB patients with known HIV status has consistently increased over the past five years from 31 per cent in 2008-2009 to 63 per cent in 2013^{4,5}. Increased access to HIV testing facilities and co-located TB and HIV testing services by both national programmes could be the reason for this improved performance at the national level. However, the HIV status of a considerable number of patients (25%) in the present study with incident TB still remained unknown, suggesting a need for better integration and co-ordination of services for effective management of HIV-TB co-infection. Other innovative measures, such as offering voluntary HIV testing for TB suspects^{4,5,24,25} need to be considered to achieve the target of ensuring that the HIV status of all TB patients is known.

The present study had certain limitations. The relevance of sputum bacillary load and radiographic severity on HIV seroprevalence were not evaluated. Sputum and body fluid/biopsy material mycobacterial culture and drug-susceptibility testing and CD4+ T-lymphocyte count were also not carried out. The patients were not followed up, and antiretroviral therapy (ART) usage and TB treatment outcomes of these patients were also not assessed. Whether the observations recorded in the present study in a medical college teaching hospital scenario could be due to referral bias or reflect the true epidemiological situation of HIV-TB co-infection needs to be confirmed in community-based studies with a large sample size.

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Conflicts of Interest: None.

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