Joint HIV/TB Collaborative Activities – What Physicians Must Know

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TB/HIV Co-infection:

The advent of the worldwide epidemic of the Human Immunodeficiency Virus (HIV) has fuelled the resurgence of Tuberculosis (TB) in some regions of the world, notably Africa and South-East Asia. TB and HIV are inextricably linked; HIV progressively weakens the immune system, making people vulnerable to a host of opportunistic infections such as TB. Moreover, the large majority of people living with HIV/AIDS (PLWHA) live in countries where the prevalence of TB is high. Actually, TB is the earliest manifestation of AIDS in over half of all cases in developing countries and accounts for about a third of AIDS deaths, and therefore is the leading killer of PLWHA in the developing world.[1]

An estimated 3.6 million persons are estimated to be living with HIV/AIDS in the South-East Asia Region in 2008.[2] As per NACO sentinel surveillance report of 2007, the prevalence of HIV infection is estimated to be 0.34 % of the population, which translates to 2.31 million people living with HIV/AIDS (PLWHA) in India (estimates revised from the earlier 5.2 million PLHAs in the country, based on the findings of the comprehensive National Family Health Survey – NFHS 3).

The HIV epidemic pattern in India, the third highest HIV burdened country, shows great variance. The worst affected states are Andhra Pradesh, Karnataka, Manipur, Maharashtra, Nagaland and Tamil Nadu. These six states have reported more than 75% of all the AIDS cases in India and are classified as High Prevalence States. Another three states namely Gujarat, Goa and Pondicherry have been classified as Moderate HIV prevalence states.[3]

Tuberculosis (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.[4] Although the TB epidemic in the country is predominantly driven by the non-HIV positive TB cases, TB mortality could well be influenced by the TB/HIV co-infection at least in certain districts in the country with high prevalence of HIV in TB patients. It has been estimated that in 2007, about 4.85% (95% CI 4.12%-5.73%) of the incident TB cases in India were HIV-positive. WHO has estimated a prevalence of 6.7% (5.5%-7.9%) of HIV in TB patients in India for 2008.[3]

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Combating TB/HIV - Conceptual Framework:

The worsening co-epidemics of TB and HIV in Asia region require urgent and effective attention. The two epidemics need a joint effort employing different, but complementary strategies. The best approach to curb the HIV epidemic is – so far – based on preventive interventions since a cure is not yet available. Prevention interventions should target all the possible ways of transmission, but especially the ones most frequently involved in the ongoing transmission in a given country. Unlike HIV, TB can be cured, even in people with HIV infection. DOTS strategy has been demonstrated to achieve TB cure rates of over 85%. A strategic framework is necessary to integrate the different interventions needed to combat the dual TB/HIV epidemic and to avoid already scarce available resources (Figure 1).[1]

HIV/TB Collaborative Activities:

TB-HIV collaborative activities between Revised National Tuberculosis Control Programme (RNTCP) and National AIDS Control Programme (NACP) started initially in the year 2001, in the six states with high prevalence of HIV/AIDS and were extended to 8 additional states in 2004. The National Framework for Joint TB/HIV Collaborative Activities was first developed in 2007, with a revision in February 2008. The overall purpose of the National framework is to articulate the policy for strengthening TB/HIV collaborative activities between RNTCP and NACP, resulting in reduction of TB and HIV burden in India.

The 2007-2008 National Framework extended basic

TB-HIV activities nationwide. The 2009 revision of the National Framework establishes uniform activities at ART (Anti retroviral Treatment) centres and ICTCs (Integrated counseling & testing Centre) nationwide for intensified TB case finding and reporting, strengthens joint monitoring and evaluation with specified national TB/HIV programme indicators and performance targets.[4]

Objectives of the framework:

1. To strengthen the mechanisms for coordination between RNTCP and NACP at National, State and District levels.
2. To decrease morbidity and mortality due to tuberculosis among persons living with HIV/AIDS.
3. To decrease the impact of HIV in tuberculosis patients and provide access to HIV related care and support to HIV- infected TB patients.

Specific TB/HIV collaborative activities:

1. Establish/Strengthen NACP-RNTCP coordination mechanisms at national, state and district level.
2. Scaling up of **Intensified TB/HIV Package of Services** across the country.
3. Joint Monitoring and Evaluation including standardized reporting shared between the two programmes.
4. Training of the programme and field staff on TB/HIV
5. **TB and HIV service delivery coordination**

5.1. Offer of **HIV testing to TB patients**

5.2. **Intensified TB case finding** at ICTCs, ART and Community Care Centres (CCCs)

5.3. Linking of HIV-infected TB patients to NACP for HIV care and support (including ART) and to RNTCP for **TB treatment**

5.4. Provision of **Cotrimoxazole Prophylactic Treatment (CPT)** for HIV-infected TB patients

6. Implementation of feasible and effective **infection control measures**
7. Involvement of NGOs/CBOs and affected communities working with NACP and RNTCP for all activities on TB/HIV collaboration.
8. **Operational research** to improve the implementation and impact of TB/HIV collaborative activities.[3,4]

Scaling up of Intensified TB/HIV Package of Services:

The Intensified TB-HIV package is being scaled up in a phased manner to cover the entire country by 2012. The Intensified TB/HIV package of services started in 2008 in 9 HIV high prevalence states (Andhra Pradesh, Goa, Karnataka, Maharashtra, Manipur, Mizoram, Nagaland, Pondicherry and Tamil Nadu), and in 2009 were extended to 9 additional states (Delhi, Gujarat, Punjab, Rajasthan, Kerala, Assam, West Bengal, Orissa and Chandigarh).[3] The package is designed to enhance identification of HIV-infected TB cases, linking to HIV care and support and monitoring of TB HIV collaborative activities. (Table I).[4]

Table I: Core TB/HIV activities for all settings, and additional activities under the Intensified TB/HIV Package

All States	Intensified TB-HIV Package States
District and State-Level Coordination between NACP and RNTCP	No additional requirements
Training of programme officials and field staff on TB/HIV	Addition: Extra training on Intensified TB-HIV package for programme and field staff
Intensified TB Case Finding at all ICTCs, ART Centres, and Community Care Centres	No additional requirements
Referral of HIV-infected TB patients to NACP for additional care and support, including cotrimoxazole prophylactic treatment and antiretroviral treatment	Addition: Decentralized provision of **cotrimoxazole prophylactic treatment (CPT)** to HIV-infected TB patients from all peripheral health institute
Referral of TB patients for HIV-testing based on HIV risk factors (selective referral)	Addition: Routine referral of **all TB patients** for voluntary HIV counselling and testing
Core TB/HIV recording and reporting from RNTCP (PMR)	Addition: Expanded TB/HIV recording and reporting NACO MIS and by RNTCP (CF and RT reports)

TB and HIV service delivery coordination:

1. HIV testing of TB patients:

In states implementing Intensified TB-HIV Package, the policy of routine offer of HIV counselling and voluntary testing to all TB patients has been adopted. This referral should be done as soon as possible after diagnosis, and results should be communicated back to the referring provider in order to provide better patient management. Eventually all the states would be covered under the Intensified Package.

HIV testing should be done by NACP at ICTCs (or any PHI where NACP HIV counselling and testing is offered). Patients who are screened for HIV through NACP whole-blood testing and are found to be HIV-negative do not require further testing. If whole blood testing results are reactive/positive, then the patient should be referred on priority to an NACP ICTC for confirmatory diagnosis.[4]

When to declare a person HIV positive?

At **NACP ICTC** the following procedures should be practiced-

The serum sample is first tested with a Rapid test.

Any reactive sample is retested using a different assay

Serum found reactive on the second assay is repeated for the third test.

Serum found reactive on all the three tests is considered HIV antibody positive.

Indeterminant result, i.e. serum that remains discordant in the second assay or reactive on the 1st and 2nd test but non-reactive on the 3rd test is considered to be indeterminate. In such cases, the person must be asked to report for a re-test after a minimum period of 2 weeks and if still indeterminate may be subjected to a confirmatory assay like Western Blot or Line Immunoassay. In some cases, the person may be followed up for 3, 6 or 9 months.[5]

2. Intensified TB case finding at ICTCs, ART and CCCs:

ICTCs

All ICTC clients should be screened by the ICTC Counsellors for the presence of the symptoms of TB disease (at pre, post, and follow-up counselling). All clients who have symptoms or signs of TB disease, irrespective of their HIV status, should be referred to the nearest facility providing RNTCP diagnostic [Designated Microscopy Center (DMC) where 2 sputum samples – on the spot & early morning – should be examined] [6] and treatment services.[4]

In all ICTCs in all States, referrals of TB suspects should be recorded on the ICTC line list to facilitate coordination with RNTCP to determine TB diagnosis and initiation of DOTS of the referred patients.[4]

The year 2009 saw continued rise in the quantum of referrals across the programme. In 2009, in the 9 States implementing the Intensified TB-HIV package, more about 315111 TB suspects were referred from ICTCs to RNTCP and of them about 33509 were diagnosed as having TB (Figure 2). In the same period, about 258037 TB patients (55% of total TB patients registered) were tested for HIV and of them about 31058 were diagnosed as HIV positive. In the past year, the proportion of TB patients with known HIV status increased from 34% to 62% (Figure 3).[3] Figure 4 and 5 highlights such referrals in Maharashtra during January to November 2008.[7]

ART Centres

HIV-infected persons attending ART centres for pre-ART registration have a high prevalence of TB disease. The incidence of TB disease among ART clients is also very high, even among clients taking ART. While ART reduces the risk of TB disease, this risk is still remains many times higher than the general population. HIV-infected clients with undiagnosed and untreated TB can be expected to seek care in ART or CCCs, posing the risk of exposing other HIV-infected persons to TB. Hence intensified TB case finding at ART centres is very important for early suspicion and diagnosis of TB disease, and for the prevention of transmission of TB infection to other clients. The TB suspects identified at ART centers/CCCs **should be prioritized and fast tracked** for evaluation by the SMO/MO in order to minimize opportunities for airborne transmission of infection to the other PLHIV at the facility.[4]

In all ART Centres in all States, referrals of TB suspects should be recorded on the ART TB-HIV line list to facilitate coordination with RNTCP to determine TB diagnosis and DOTS initiation. [4]

3. Referral of HIV-infected TB patients to NACP for care and support, including antiretroviral

treatment:

The treatment of HIV-infected TB persons should be done using RNTCP DOTS as per national policy. Early diagnosis and effective treatment of TB among HIV infected patients are critical for curing TB, minimizing the negative effects of TB on the course of HIV, and interrupting the transmission of TB infection to other persons in the community. Management of TB under RNTCP can significantly prolong the lives of HIV positive people with TB. All known HIV-positive TB patients are offered either RNTCP Category I [$2(HRZE)_3 + 4(HR)_3$] or Category II [$2(HRZES)_3 + 1(HRZE)_3 + 5(HRE)_3$] treatment, depending on their previous history of TB treatment.[5]

In addition to TB treatment under RNTCP, all HIV-infected TB patients must be provided access to care and support for HIV/AIDS, including antiretroviral therapy. ART reduces TB case fatality rates and the risk of recurrent TB. ICTC counsellors and the treating physicians should counsel these patients on the importance of ART and on the free availability of ART evaluation and treatment.[4]

Data on linkage of HIV-infected TB patients to HIV care has only recently become available; among the 6039 HIV-positive TB registered in 4q08, 2487 (41%) were provided ART during TB treatment.[3]

HIV-infected TB patients should be promptly referred to the nearest ART centre by the treating physicians and ICTC counsellors. This visitation of the ART centre, however, should preferably occur **at least two weeks after initiation of TB treatment;** to ensure that at least some reduction in TB transmission potential occurs among these patients prior to visitation of a clinical setting with large numbers of HIV-infected persons. TB patients referred to ART centres should be carefully educated on cough hygiene.[4]

NACO recommends that ART be given to [4,8]:

- All patients with extra-pulmonary TB (stage 4) – Start ART within 2 weeks of initiation of ATT in all patients irrespective of CD4 count **and**
- All those with pulmonary TB (stage 3) with CD4 count < 350 cells/mm^3 - Start ART within 2 weeks of initiation of ATT **(As per GOI's amendment in April 2009).** For patients with CD4 > 350 cells/mm^3, defer ART.

The current recommendations on ART are to use a triple drug combination. Ideally two drugs from NRTI group and one from NNRTI group or PI group should be included in the regimen. Compelling epidemiological and clinical evidence demonstrates that with strict adherence, the use of three drugs in combination will achieve sustained viral suppression for several years leading to improvement in quality of life and prolongation of life. A combination of, Stavudine/Zidovudine plus lamivudine plus Efavirenz/Nevirapine is usually used.[5]

Protease inhibitors and non-nucleoside reverse transcriptase inhibitors may inhibit or induce cytochrome P-450 isoenzymes and thus alter the serum concentration of Rifamycins. Rifamycins induce cytochrome P-450 and substantially decrease blood levels of these antiretroviral drugs. Dose adjustments for Nevirapine co-administered with Rifampicin has not been established. Hence, co-administration of Rifampicin with any of the protease inhibitors (Ritonavir, Indinavir, Nelfinavir) or non-nucleoside reverse transcriptase inhibitors (Nevirapine) should be avoided.[5, 9]

All TB patients co-infected with HIV should be treated with a Rifampicin containing treatment regimen under DOTS. In TB patients co-infected with HIV, TB treatment should be completed prior to starting ART, unless there is a high risk of HIV disease progression and death during the period of TB treatment (i.e., a CD4 count< 250/mm^3 or the presence of disseminated TB). In a patient who has been on treatment with Rifampicin, at least 2 weeks should have elapsed after the last dose of Rifampicin before starting protease inhibitor or non-nucleoside reverse transcriptase inhibitors. This time gap is necessary for reduction of the enzyme inducing activity of Rifampicin prior to commencement of antiretroviral drugs.[9]

In patients with very low CD4 counts requiring concomitant administration of ART and anti-TB treatment, the ARV regimen should be modified by replacing Nevirapine with Efavirenz. On completion of TB treatment such patients can be switched back to Nevirapine.[5, 9]. EFV should be avoided in the first trimester of pregnancy because of the risk of teratogenicity. When NVP is used in pregnancy, close monitoring of liver function is required.[8]

4. Provision of cotrimoxazole preventative

treatment (CPT) for HIV-infected TB:

CPT has been shown to reduce mortality among HIV-infected TB patients, and is recommended by NACP for all HIV-infected patients. All HIV-infected TB patients should therefore be provided CPT. At a minimum, monthly provision of CPT should be available at all ART centres for the benefit of those patients who are able to return to the ART centre on a monthly basis.[4]

In States implementing Intensified TB/HIV package, CPT should also be made available for HIV-infected TB patients at all peripheral health institutions having a Medical officer and an institutional DOT centre, using RNTCP mechanisms. In this mechanism, CPT is delivered by the peripheral health institute staff, and not community DOT providers, to maintain confidentiality regarding HIV status within the health-care system.[4]

Data on linkage of HIV-infected TB patients to HIV care has only recently become available; among the 6039 HIV-positive TB registered in 4q08, 4098 (68%) were reported to have been provided with CPT during TB treatment.[3]

Infection control practices:

Prevent spread of TB in facilities caring for HIV-infected persons[4]:

1. ART centres should not be co-located with DMC/DOT centers, and should not share waiting areas.
2. ART centres should have a well ventilated waiting & seating area.
3. Fast-tracking of chest symptomatic should be done to ensure that there are minimum chances of contact of these patients with healthy ones.
4. Health education on cough hygiene should be stressed upon.

Prevent spread of HIV through safe injection practices in facilities providing RNTCP services[4]:

Measures to reduce parenteral HIV transmission include the use of sterilized injection and surgical equipment in medical settings. Steps should be undertaken by concerned authorities to ensure the availability at all times and all facilities, of sterilized disposable needles and syringes and needle destroyers.

The priority areas for collaborative operational research with both programmes for TB/HIV include[4]:

- Reasons for loss of TB suspects referred from integrated counseling and testing centers to designated microscopy centers
- Reasons for non-initiation of ART and CPT for HIV-infected TB patients
- Causes for delay in treating HIV in TB patients, and effect of corrective actions
- Feasibility and cost-effectiveness of isoniazid preventive treatment for HIV-infected patients in ART centers
- Risk of TB among HCWs at HIV care, support and treatment centers

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Figure 1: Regional Strategic framework of interventions for TB/HIV

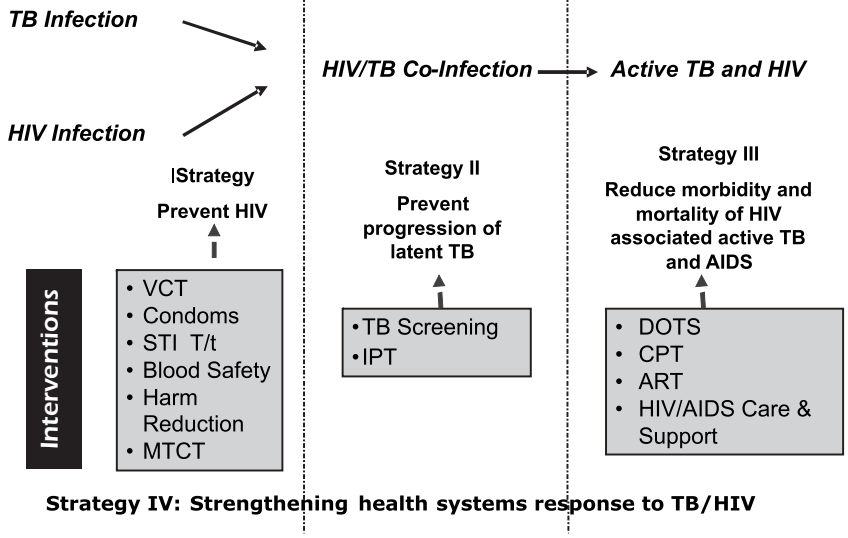

Figure 2 TB suspects referred from ICTC to RNTCP, 2006-09, (for 9 Intensified TB/HIV Package States)

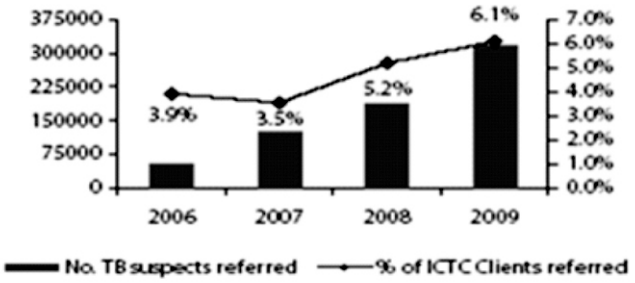

Figure 3 TB patients with known HIV status, 4q08-4q09, (for 9 Intensified TB/HIV Package States)

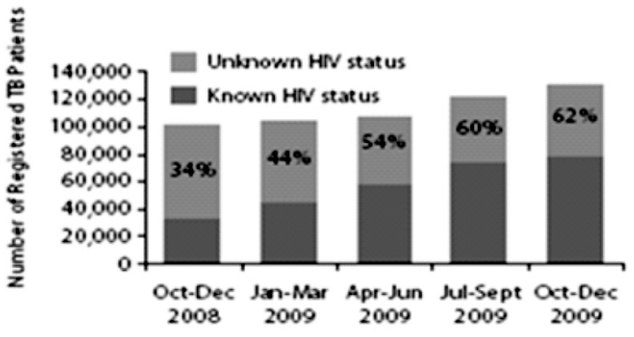

Figure 4: Referral from ICTC to RNTCP for State (Jan to Nov 08)

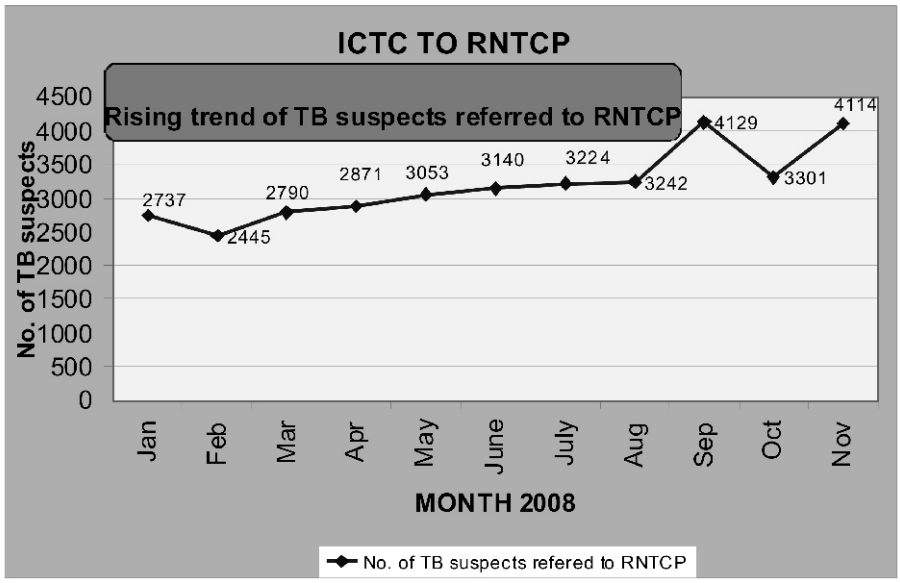

Figure 5: Referral RNTCP to ICTC for State (Jan to Nov 08)