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HIV/TB Co-Ordination Program – An Integration in Highly Epidemic Provinces

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Abstract

Tuberculosis is the commonest co-infection among PLHA (HIV/AIDS). An appropriate measure for controlling TB spread in community of high TB/HIV burden state that requires intervention strategies against this dual epidemic which include intensified case finding at ART centers, involvement of health care delivery system, and Non-Government Organizations for early detection of TB and HIV, counselling and support, provision of daily patient's weight band-wise FDD, ATT for TB, cotrimoxazole preventive/ prophylaxis therapy (CPT) and Highly active anti-Retro viral Treatment (HAART) at the integrated centers.

Keywords: HAART (highly active anti-retroviral therapy), FDD, ICTC, VCTC, (CPT)

INTRODUCTION

Koch's disease has been a major public health problem for centuries and is the leading cause of morbidity and mortality among PLHA (people living with HIV/AIDS) [1–3]. It is estimated that 2.5 million PLHA are infected in India and considering 40% of the Indian population is infected with Tuberculosis, an estimated 1 million persons are having co-infection of TB and HIV. HIV is the most common risk factor for the progression of TB and latent TB infection with TB disease. Active TB disease is the commonest opportunistic infection, and it is also the leading cause of death among People living with HIV/AIDS. HIV positivity increases 50–60% lifetime risk of developing TB disease as compared to an HIV negative status who has a lifetime risk of 10% developing TB disease. HIV/TB joint survey conducted by the Central Tuberculosis Division & National AIDS control organization has shown 1% to 13% HIV amongst TB patients [2–4] TB and HIV cost more than 30% of the annual household income in developing countries and have a substantial impact on the economy in the developing world [4]. From 1990 to 2005, It is shown by various surveys that increased incidence of TB occurred in the countries with higher adult HIV prevalence in comparison to low prevalent HIV countries [5]. The proportion of TB cases coinfected with HIV was highest in countries in the African region, exceeding 50% in parts of southern Africa [6]. In India, HIV seroprevalence among TB patients showed wide variations from state to state and even between different districts of the same state [7–13]. The risk of development of TB co-infection among HIV positive patients in India has been estimated to be nearly 7 per 100 person-years [12].

HIV presents a substantial threat to the performance of the National Tuberculosis elimination program (NTEP). Less than 1% of

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adults are currently infected with HIV, but if the prevalence of HIV infection will increase, the impact of the TB epidemic on the NTEP would be devastating [14–16]. Nationally, NTEP must be able to reverse the increase in the TB burden due to HIV. It is observed from various studies that mortality among the HIV patients associated with TB can be reduced to maximum extent if patients are given ATT together with HAART [17, 18]. For this, all TB patients must be tested for HIV. It is recommended to counsel and test HIV for every TB patient in a country with high HIV infection prevalence of 1% in the general population [19–21].

In India, NACO guidelines specify that health providers in the NTEP/DOTS clinics must offer HIV testing to all TB patients in states where TB/HIV integration program is existing [22].

HIV/AIDS and tuberculosis (TB) co-infections are also called as "deadly duo" and referred to as HIV/TB. HIV weakens immunity and leads to susceptibility to acquire TB and are amenable to develop active TB 50 times more each year than HIV-negative people.

Mycobacterium Tuberculosis may lead to the progression of HIV to AIDS. Mycobacterium Tuberculosis also produces latent TB infections among few cases that is asymptomatic stages unsimilar to active TB in which patient neither are considered sick nor they can excrete Tuberculous bacilli and cannot spread infection to others but weaker immunity or immunocompromised conditions, like diabetes, malaria, corticosteroid therapy or HIV infection, may produce recurrent illness after conversion of latent TB to active TB or may infect them easily from new TB infections [23]. Latent TB is also known as Dormant TB usually causes slow growing Mycobacteria. Active TB infection possesses all symptoms of TB and is communicable infection especially have public health importance and cause of fatality among PLHA. 5.8 million people are newly diagnosed with TB and reported worldwide in 2020. Each year – 8 million to 10 million new people contract TB and 2 million dies from it. Only about 10 percent of people with TB develop active TB during their lifetimes but this percentage is increasing – largely due to the increased infections among people with HIV/ AIDS [24].

Nearly 40 million people are living with HIV infection worldwide and as many as one-third are co-infected with TB. Most TB cases in people living with HIV/AIDS occur in sub-Saharan Africa, where up to 80 percent of TB patients may be co-infected with HIV.

Without proper treatment, 90 percent of people living with HIV die within months of contracting TB is the leading cause of death for people with HIV/AIDS in Africa and one of the leading causes of death worldwide [25]. HIV imposed severe threat on TB cases which becomes the most common cause of fatality among associated infections. Latent TB infection if treated with preventive regime may reduce disease progression. These patients require ATT as per the tire history of categories, Rifampicin sensitivity status, resistant nature of TB.

DIAGNOSING AND TREATING ADULTS WITH HIV/TB CO-INFECTION

TB is difficult to diagnose in people living with HIV because the commonly used diagnostic tools are less able to detect the TB bacteria in them. People with HIV are more likely to develop TB both inside and outside of the lungs, also making the diagnosis more difficult, and the disease more deadly.

Looking at coughed up sputum under a simple light microscope is the most widely used diagnostic tool for TB in resource poor settings. The test is more than 100 years old and detects fewer than 60 percent of all new TB infections and as few as 20 to 35 percent of HIV/TB infections. Countries, like the US and Europe, replaced these outdated methods with better tests decades ago, and today have a small fraction of the cases of TB as do poorer countries.

Active TB can be treated and cured in people with HIV/TB, if it is diagnosed and treated before the disease becomes too severe. Firstline ART consists of isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin (RHEZS).

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The TB drugs being used today were discovered in the 1950's, require 6–9 months of continued treatment to be effective and have serious liver toxicity issues. A new TB therapy has not been developed for more than 40 years.

Successfully treating HIV/TB treatment is complicated. There are drug-to-drug interactions between the complex drugs regimens required to treat both diseases, and paradoxically, people with HIV/AIDS can develop something called Immune Reconstitution Inflammatory Syndrome (IRIS), an over-reaction of the immune system that inflames TB. Studies are underway to determine the best antiretroviral drugs to administer, how to manage Immune reconstitution inflammatory syndrome (IRIS), and the optimal duration of TB treatment in HIV patients. These studies are critically important because successful TB treatment can prolong the lives of people with HIV by at least two years and probably longer if they get started on AIDS medicines.

If someone has been exposed to TB, but is not yet sick, active TB can be prevented with a 6 to 9-month course of TB preventive therapy. Preventive therapy reduces the risk of people with HIV/TB developing active TB by as much as 60 percent.

Special Considerations for Children with TB/HIV

Children are extremely vulnerable to contracting TB from adults in the household. TB is not usually transmitted from child to child.

Children 5 years old and younger are at very high risk for developing active TB because the immune system is less developed. Children with HIV are at increased risk for contracting TB and specifically for developing TB meningitis, which often results in deafness, blindness, paralysis, and mental retardation.

Diagnosis of TB in children is difficult because most children are unable to develop enough sputum for the laboratory to confirm TB infection. Pediatric drug formulations are not available for TB and few are available for HIV.

The Threat of Drug Resistance

Drug resistance impedes killing of *Tubercle bacilli*. Drug resistance usually develops among PLHA most commonly because of malabsorption of drugs, weakening of immunity which reduces the effect of ATT among them, incomplete treatment of ATT, substandard drugs or lesser dose of ATT. MDR-TB equally poses threat among PLHA as its treatment is not only complicated, but it also does not spread regular Tuberculosis. Contacts or at-risk population who got infections from MDR develop drug resistant Tuberculosis. MDR cases who are at least resistant to both Rifampicin and Isoniazid or more drugs and XDR-TB includes Fluroquinolone group and Second-line injectables usually sometime needs more complicated and expensive and TB strategies regimen like short duration (Bedaquiline, Pretomanid/Delamanid, linezolid,) and long duration therapies (Levofloxacin/Moxifloxacin, Bedaquiline, Linezolid, Clofazimine and Cycloserine).

TB-HIV Integration Program in Higher Prevalence State of India

Tuberculosis and HIV co-existence are increasing worldwide which leads to more conversion and activation of dormant-Latent type of Tuberculosis. India places second after South Africa in terms of the absolute number of people living with HIV/AIDS, globally. This condition increases more incidence of primary and newer Tubercular infection, recurrence of Tuberculosis and re-activation of Tuberculosis which requires implementation of TB-HIV integration program in high TB-HIV adult prevalence states.

Voluntary Counseling and Testing to TB Patients

India has adopted the policy of voluntary HIV counseling and testing to all TB patients with unknown HIV status and not to those with known HIV status or HIV negative status within past six months at the nearest Integrated counselling and testing center.

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The referral of patients is mandatory, but testing is voluntary. This referral can be done any time after the diagnosis of TB, during or after initiation of the Anti TB treatment. Also sending patients for diagnosis and testing of TB among PLHA is mandatory. After getting consent for VCT, patient must complete standard "ICTC referral form" and refer to ICT center.

Shared of Confidentiality of HIV Status

Confidentially sharing of HIV status among physicians treating patients and other staff of health care system is necessary but confidentiality must be maintained to other persons outside the health care system.

Cotrimoxazole (Sulfamethoxazole and Trimethoprim) Preventive Therapy (CPT) to All HIV-Infected TB Patients

FDC of CPT is provided to All NIKSHAY enrolled coinfection patients under NTEP irrespective of their CD4 counts.

Referral of HIV Infected TB Patients for Highly Active Anti Retro Viral Treatment (HAART)

Most TB pulmonary and extra pulmonary patients with HIV are referred to as HAART with ATT which is entirely based on NACP-ART guideline (24).

Global Impact of HIV/TB Co-Infection Epidemic

Individuals infected with latent tuberculosis have an approximately 10% lifetime risk of developing active TB, compared to 60% or more risk of development of active TB in persons dually infected with HIV. TB reduces quality of life, makes HIV progress to complexify and deadly AIDS, and increases mortality and longevity among PLHA. It is estimated that 3.5% of TB cases also have HIV co-infections, roughly.

Regarding the prevalence of TB in HIV positive patient, on an average 5–15% of HIV positive patients attending Voluntary Counseling and Testing Centers (VCTCs) have pulmonary TB.

Central TB division & the national AIDS control Organization have adopted the policy of routinely offering voluntary HIV counseling and testing to all TB patients as part of an intensified TB/HIV package of services for the states with the highest HIV burden

Diagnosis of TB-HIV and Opportunistic Infections

Pulmonary TB is the commonest form of TB. The clinical presentation of TB depends upon the degree of immuno-suppression in the patient. The presentation of TB in early stages of HIV infection is like that in HIV negative patients often resembling post-primary pulmonary TB with upper lobe disease, cavitary lesions and sputum smear results are often positive. During the later stages of HlV infection the presentation of TB often resembles primary disease with infiltrative lesions, lower lobe disease, intrathoracic lymphadenopathy and the sputum smear results are often negative. The reported case rates of smear negative pulmonary TB have increased following the TB-HIV co-epidemic.

The clinical manifestations in a TB patient that suspects HIV infection: Oral/Esophageal candidiasis, Chronic diarrhea more than one month, Weight loss more than 10% of the body weight in the last 6 months period, Fever for more than one month, Herpes Zoster, Recurrent pneumonia, Typhoid, Oral hairy leukoplakia, Present or past genital ulceration, Kaposi's sarcoma, and Generalized dermatitis.

The detection of HIV infection in TB patients can be achieved by referring the patients to VCTCs. VCTCs are the portals of entry for individuals for the diagnosis of HIV infection.

VCTCs are the key points for a range of interventional activities towards HIV prevention and care.

Tests of HIV Infection

The first test is performed by Combaids kit (screening test) and if it is positive a 2nd test is performed by Capillus kit and if the 2nd test is positive the 3rd test is performed using the Tridot kit. If all the 3 tests are positive, the person is declared as positive for HIV infection.

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HIV positive patients with anyone of the following symptoms should be suspected of having TB and investigated further:

Cough of duration of 3 weeks or more, Fever of more than 2–3 weeks Weight loss Fatigue, restlessness, Unexplained dyspnea or chest pain, Hemoptysis, Lymph node enlargement (especially localized enlargement), Headache, vomiting, alteration of sensorium or convulsions.

Patients who are HIV positive should be referred to the health care facilities implementing the revised National Tuberculosis Control program (RNTCP), recently known as NTEP for the diagnosis of TB.

Treatment of TB/HIV Co-Infection

Till date no cure is available for HIV/AIDS. It is only the opportunistic infections emanating from the disease that can be treated. Category for TB patients are similar irrespective of the HIV status. Thus TB-HIV infected individuals receive Category-l (Treatment with Rifampin (RIF), Isoniazid (INH), Pyrazinamide (PZA), and Ethambutol (EMB)) treatment, if they are new smear positive cases, smear negative with extensive parenchymal involvement or severe forms of extra pulmonary TB.

The response to treatment is same in terms of clinical, radiological and microbiological improvement to the short course chemotherapy irrespective of the HIV status of the individual. However, the case fatality among TB-HIV infected patients is higher compared to HIV negative patients both during and after anti-TB treatment. The antiretroviral drugs are however too expensive and have serious side effects, drug interactions.

WHO and UNICEF recommend that asymptomatic HIV infected children should receive BCG vaccination as per the immunization policies but should be withheld in a child having symptomatic HIV infection, BCG when given to a symptomatic HIV positive individual would lead to disseminated BCG disease

Management and Prevention of TB Among HIV Patients

This is largely based on globally recommended guidelines of three I's (3-I's)

1. *Intensified Case Finding (ICF):* Every HIV patient must be evaluated for TB if they have symptoms of TB. Every TB positive patient is expected to early detect HIV within 2–4 week of TB positivity in high prevalence HIV states. Care, support and treatment (CST) is the policy package component of AIDS Control Program [26].

TB patients are categorized as:

i. Rifampicin sensitive status considered as unknown or known,
ii. Category-I/ category-II/ MDR-TB/ XDR-TB status as per previous ATT drug history.
iii. Initiation of fixed dosage daily ATT regimen as per categorization.
iv. Offering of ART/HAART among HIV-TB irrespective of CD4+ cell count as soon as TB treatment is tolerated (between 2 weeks to 2 months) to sustain reduction in HIV viral load, increased CD4+ counts and decreased defining illness and mortality. It can also facilitate immunological reconstitution and decreased AIDS complications and co-infections.
v. Sometimes concurrent ATT and HAART regimen may lead to paradoxical reactions (immune reconstitution inflammatory syndrome also known as IRIS) which is exhibited by increased signs and symptoms of radiographic manifestation of TB and include high grade fever, lymphadenopathy, increased intra-thoracic lesions and worst radiographical findings. These findings must be differentially diagnosed with the treatment failure of ATT as it is the result of restitution and reconstitution of immunity which leaded the hyper-responsiveness and hyper-sensitivity and induced transient acute immune-inflammatory response. This transient immuno-inflammatory response sometimes, especially when it takes it's severe and complex forms, needs corticosteroid remedy.

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2. *Isoniazid Preventive Therapy for PLHIV/AIDS:* Isoniazid preventive therapy is advised for prevention of incident TB among HIV infective cases. This regimen protects latent TB infection progression to active TB, also it prevents re-infection and new infections. This therapy is successful among asymptomatic TB individuals and among CLHIV/AIDS (children living with HIV/AIDS). The advantage of IPT is that PLHA does not have the concern of development of INH resistance.
3. *Infection Control:* Infection control requires proper prevention of TB; it is progression and prevention and control of other co-infections of TB-HIV infection. In addition to care, support and treatment cotrimoxazole preventive therapy is recommended to reduce mortality and prevent opportunistic infections of PLHIV [27].

CONCLUSIONS

The HIV epidemic has posed major challenges to TB control efforts. Preventing HIV associated with TB entails full implementation of DOTS and primarily preventing HIV infection through ART. It is necessary that both the TB and HIV control programs work together to contain the spread of both these infections. An action plan on TB-HIV program coordination has been formulated between the Central TB Division and the National AIDS Control organization. However, the linkages between the NTEP and the VCTC are still in the nascent stage and optimal co-ordination between the two programs is necessary to curb dual epidemics. Currently a joint project of the National Tuberculosis institute and the WHO is underway in the implementation of TB-HlV collaborative activities in the Mandaya district, The experiences gained from this study would stand in good stead for implementing collaborative activities in the areas of mutual concerns shared by the two programs.

However, willingness to be tested does not necessarily mean acceptance of and undergoing testing for HIV. It is therefore important to address issues that could adversely influence HIV testing among TB patients. Recruitment of counsellors at TB clinics could help to motivate and prepare patients on the need for HIV testing. Accessibility of VCT center and patient-centered counseling at the VCT center could help in further motivating TB patients to undergo testing for HIV. With the roll-out of ART, TB clinics are likely to play a crucial role as entry points for HIV care and support.

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