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TB-HIV CO-INFECTION IN INDIA

Preetish S. Vaidyanathan[1] & Sanjay Singh[2]

INTRODUCTION

According to the National AIDS control organization, about 3.82-4.58 million Indians were estimated to be infected by HIV at the end of the year 2002[1]. The HIV prevalence in the population between 15-49 years of age, in India, is relatively low at 0.75%[2]. However, due to its large population, India ranks second after South Africa in terms of the absolute number of people living with HIV/AIDS. India has the largest number of tuberculosis (TB) cases in the world. India shoulders about 14 million cases of TB and it is estimated that about 1.8 million incident cases of TB occur in India every year of which 0.82 million are highly infectious smear positive cases. TB was declared a global emergency in the year 1993 and recently the Director General of WHO has declared AIDS also as a global emergency. There exists a synergistic relationship between TB and HIV. The interface between TB and HIV is increased in countries like India where both TB and HIV infection are maximally prevalent in people of 15-49 years of age. Also, the socio-economic factors of poverty, ignorance and stigma are common to both the diseases. Thus the TB and HIV/AIDS control progammes share mutual concerns.

This article deals with various issues related to TB-HIV co-infection in India.

Impact of HIV infection on the TB epidemic

The HIV epidemic has the potential to worsen the TB situation as has happened in certain African countries. HIV is the most potent risk factor for the progression of TB infection to active disease. Individuals infected with M.tuberculosis have an approximately 10% life time risk of developing active TB, compared to 60% or more in persons dually infected with HIV and TB. Most cases of TB in HIV infected patients are due to endogenous reactivation though HIV infection also greatly increases the risk of developing TB following new infection. However, this aspect in India requires to be studied further. In developing economies like India the potential financial burden imposed by TB cases attributable to HIV infection could overwhelm budget and support services.

Impact of TB infection on the HIV epidemic

TB is the most common serious opportunistic infection in HIV positive patients and is the manifestation of AIDS in more than 50% of cases in developing countries[3]. Also to be noted are the facts that TB shortens the survival of patients afflicted with HIV infection, may accelerate the progression of HIV and is the cause of death in one third of people with AIDS world wide. The higher mortality is due to the progression of AIDS rather than TB probably due to the fact that *M. tuberculosis* increases viral replication.

Magnitude of TB-HIV co-infection in India

There is no official data on the magnitude of the TB/HIV co-infection in India. However, the data garnered from studies on HIV seropositivity among adult TB patients in tertiary health care centers does provide an insight on the magnitude of the problem though it would be naïve to assume the data to be representative of the problem in the community. These studies were conducted at different times in different centers. The findings of these studies have been summarized in Table 1.

1. Chief Medical Officer, 2. Field Investigator, National Tuberculosis Institute, No.8, Bellary Road, Bangalore - 560 003
Address for correspondence: Dr Preetish S Vaidyanathan, Chief Medical Officer, National Tuberculosis Institute, No. 8, Bellary Road, Bangalore - 560 003, Karnataka. Tel: 080-23441192/3, **Email :** ntiindia@blr.vsnl.net.in

Table 1. Prevalence of HIV infection among tuberculosis patients

Place	Year	No. of TB patients examined*	HIV +VE in %
Delhi[4]	Sep. 1997 - Aug. 1998	1,409	1.14
Delhi[5]	1994-1999	500	0.4
Delhi[21]	1994-95	1002	0.5
Lucknow[6]	Aug. 1994 - Dec 1996	988	1.42
Lucknow[7]	1995 - 1996	400	1.25
	1996 - 1997	225	1.78
	2000 - 2001	350	4.28
Ajmer[8]	July 1993 - June 1995	2448	0.7
Pune[9]	July & August 1995	400	10.00
	Jan & Feb 1996	400	15.75
	July & August 1996	400	21.25
	Jan & Feb 1997	400	21.50
	Jan & Feb 1998	400	23.25
	Jan & Feb 1999	400	22.25
	Jan & Feb 2000	400	28.75
Pune[16]	1991	344	3.20
	1992	187	5.90
	1993	395	5.0
	1994	1046	10.0
	1995	1189	15.50
	1996	1457	20.10
	Total	4618	15.0
Pune[17]	1995	1256	12.1
Goa[10]	1995	1044	2.01
	1996	1133	4.14
	1997	1071	5.22
	1998	1004	6.77

Place	Year	No. of TB patients examined*	HIV +VE in %
Goa[10]	1999	929	6.35
	2000	980	10.91
	Total	6161	5.81
Indore[11]	N.A	100	4.00
Pondicherry[12]	1994	500	4.00
	1995	550	3.50
	1996	550	4.90
Thanjavur[13]	1996	510	0.59
	1999	405	8.89
Aligrah[14]	1996-97	1006	0.8
	1997-98	1215	0.91
	1998-99	1126	1.24
	1999-2000	1330	1.8
	2000-2001	1204	2.82
Mumbai[15]	1988-89	468	2.60
	1989-90	707	2.70
	1990-91	641	3.90
	1991-92	678	9.60
	1992-93	596	9.90
	1993-94	788	10.20
	Total	3878	26.70
Chennai[18]	1991	392	0.8
	1992	680	1.30
	1993	358	3.40
	Total	1430	1.70
Chennai[19]	1996	112	17.0
Aurangabad[20]	1995-96	340	4.7

* The type of TB cases (smear positive/negative, extra pulmonary) have not been specified by many authors. Hence the data presented here does not mention the type of case.

In Asia where HIV epidemic is at an early stage, surveillance data show that the rates of HIV infection had remained lower in-patients with TB compared to that seen in Africa[22]. Studies form Uganda and Zambia have recorded HIV rates of 50-70% among TB patients[23]. In Tanzania, the survey conducted during 1994-1998 on 10,612 new smear positive TB patients revealed 40% HIV prevalence[24]. HIV sero-prevalence rates among patients with extra-pulmonary TB are even higher[22]. Extra pulmonary TB has been reported in upto 70% of HIV related TB cases when the CD4 lymphocyte counts falls below 10025. However, the studies enumerated in the table above indicates that the HIV sero-positivity in TB patients show a wide variation ranging from 0.4% in a study in Delhi to 28.75% in a study conducted in Pune. Moreover, periodic studies from some centres indicate that the HIV prevalence is rapidly increasing among TB patients.

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

Diagnosis of TB-HIV co-infection

TB can occur at any time during the course of HIV infection. Even in HIV infected patients, 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 similar to that in HIV negative patients often resembling post-primary pulmonary TB with upper lobe disease, cavitatory lesions and sputum smear results are often positive. During the later stages of HIV infection the presentation of TB often resembles primary disease with infiltrative lesions, lower lobe disease, intra thoracic 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. There is a lack of a 'gold standard' diagnostic tool for smear negative pulmonary TB. It is often difficult to distinguish other HIV related pulmonary disease from pulmonary TB. Hence the extent of over diagnosis of smear negative pulmonary TB is uncertain. It is important to follow the diagnostic algorithm outlined for the diagnosis of pulmonary TB even in HIV positive individuals in order to diagnose smear negative TB.

The following conditions in a TB patients should arouse the suspicion of HIV infection:

- Oral/Oesphageal candidiasis
- Chronic diarrhea more than one month
- Weight loss more than 10% 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 sarcome
- Generalized dermatitis

The detection of HIV infection in TB patients can be achieved by referring the patients to VCTCs. The VCTCs are the portals of entry for individuals for the diagnosis of HIV infection. VCTCs are the key entry points for a range of interventional activities towards HIV prevention and care. The rapid HIV test kits consisting of 3 different antigens are used for the diagnosis 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.

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, listlessness
- Unexplained dyspnoea or chest pain
- Haemoptysis
- 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 programme (RNTCP) 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. Anti retroviral drugs used to treat HIV/AIDS are effective in slowing down the action of the virus and prolong the life of patients. The treatment for TB is same for HIV infected as for non-HIV infected TB patients. The same criteria determine the treatment category for TB patients irrespective of the HIV status. Thus TB-HIV infected individuals receive Category-I treatment if they are new smear positive cases, smear negative with extensive parenchymal involvement or severe forms of extra pulmonary TB. WHO recommends that people with TB/HIV complete their TB therapy prior to beginning anti retroviral treatment unless there is a high risk of HIV disease progression and death during the period of TB treatment (CD4 count <200/ml or the presence of disseminated 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. Approximately 30% of HIV infected, smear positive TB patients die within 12 months of starting treatment and about 25% of those who complete treatment would die during the next 12 months[25]. Largely this can be attributed to other HIV related problems like septicaemia, diarrhea, pneumonia, anaemia, Kaposi's sarcoma and cryptococcal meningitis, though to an extent this could be due to TB itself. Multidrug resistant TB is common in patients with HIV infection[26]. HIV infection itself does not cause multi drug resistant TB but it fuels its spread by increasing susceptibility to infection and acceleration of TB infection to disease.

Co-administration of rifampicin with certain class of antiretroviral drugs (protease inhibitors or non-nucleoside reverse transcriptase inhibitors is contraindicated). This is because protease inhibitors or non-nucleoside reverse transcriptase inhibitors may inhibit or induce cytochrome P-450 isoenzymes and these drugs may alter the serum concentration of rifamycins. Rifamycins induce the hepatic cytochrome P-450 isoenzymes and may substantially decrease the blood levels of the antiretroviral drugs resulting in the potential development of resistance to these drugs. In case protease inhibitors or non-nucleoside reverse transcriptase inhibitors are used, at least two-weeks should elapse after the last dose of rifampicin. The antiretroviral drugs are however too expensive and have serious side effects. They are currently not available under the National AIDS Control Programme. The antiretroviral therapy for the treatment of TB-HIV co-infection is outlined in Table 2.

Table 2. Antiretroviral therapy for individuals with tuberculosis co-infection[27] (WHO recommendations - April 2002)

Situation	Recommendations
Pulmonary TB and CD4 count <50/mm^3 or extrapulmonary TB	Start TB therapy. Start one of these regimens as soon as TB therapy is tolerated : ● ZDV/3TC/ABC ● ZDV/3TC/EFV ● ZDV/3TC/SQV/r ● ZDV/3TC/NVP
Pulmonary TB and CD4 50-200/mm^3 or total lymphocyte count <1000-1200/mm^3	Start TB therapy. Start one of these regimens after 2 months of TB therapy : ● ZDV/3TC/ABC ● ZDV/3TC/EFV ● ZDV/3TC/SQV/r ● ZDV/3TC/NVP
Pulmonary TB and CD4 >200/mm^3 or total lymphocyte count >1000-1200/mm^3	Treat TB. Monitor CD4 counts if available. Start ART.

ZDV - Zidovudine
3TC - Lamivudine
ABC - Abacavir
EFV - Efavirenz
NVP - Nevirapine
SQV/r - Saquinavir/low dose ritonavir

BCG vaccination and HIV infection

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.

CONCLUSION

The HIV epidemic has posed major challenges to TB control efforts. Preventing HIV associated TB entails full implementation of DOTS and also primarily preventing HIV infection. It is necessary that both the TB and HIV control programmes work together to contain the spread of both these infections. An action plan on TB-HIV programme coordination has been formulated between the Central TB Division and the National AIDS Control organization. The purpose of the coordination is to ensure optimal synergy between the two programmes for the prevention and control of both the diseases[28]. However, the linkages between the RNTCP and the VCTC are still in the nascent stage and optimal co-ordination between the two programmes is necessary to curb the dual epidemics. Currently a joint project of the National Tuberculosis Institute and the WHO is underway in the implementation of TB-HIV collaborative activities in Mandya 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 programmes.

LIST OF REFERENCES

1. Website http://www.naco.nic.in/indiascene/esthiv.htm. **Date accessed on 21st Dec, 2003.**

2. National AIDS prevention and control policy, National AIDS Control Organization, Ministry of Health and Family welfare, Government of India.

3. UNAIDS.AIDS epidemic update, **December 2001. UNAIDS Geneva 2001.**

4. Jain SK, Aggarwal JK, Rajpal S & Baveja U: Prevalence of HIV infection among tuberculosis patients in Delhi - A sentinel surveillance study. **Ind J TB 2000; 47, 21-26.**

5. Sharma SK, Saha PK, Yogita Dixit, Naveen H, Siddaramaiah, Pradeep Seth & Pandey JN : HIV seropositivity among adults tuberculosis patients in Delhi. **Ind J Chest Dis & Allied Sci; 2000, 42, 157-160.**

6. Kulshershtha R, Nigam M, Sarin S & Mathur A: Prevalence of AIDS among tuberculosis patients in Lucknow. **Indian J Med Microbiology; 1997, 15, 79-81.**

7. Prasad R, Saini JK, Kannaujia RK, Sarin S, Suryakant, Kulshreshth R, Nag VL & Tripathi AK: Trend of HIV infection in patients with pulmonary tuberculosis in Lucknow area. **Ind J TB; 2003, 50, 39-41.**

8. Purohit SD, Gupta RC & Bhatara VK : Pulmonary tuberculosis and HIV infection in Ajmer. **Lung India; 1996, 14, 113-120.**

9. Tripathi S, Joshi DR, Mehendale SM, Menon P, Joshi AN, Ghorpade SV, Patil U & Paranjape : Sentinel surveillance for HIV Infection in tuberculosis patients in India. **Ind J TB, 2002, 49, 17-20.**

10. Lalita Fernandes, Durga Lawande & Mesquita AM: Prevalence of HIV infection among tuberculosis patients in Goa. **Ind J TB 2002, 49, 35-236.**

11. Khare KC: HIV seropositivity in pulmonary tuberculosis patients in Indore, Madhya Pradesh. **Ind J TB 2001, 48, 153-156.**

12. Vasudvaiah V: HIV infection among tuberculosis patients. **Ind J TB 1997, 44, 97-98.**

13. Rajasekharan S, Uma A, Jeyaganesh D, Senthamizhchlevan A, Sarin S & Gopinathan: Trend of HIV infection in patients with tuberculosis in rural south India. **Ind J TB; 2000, 47, 223-226.**

14. Zuber Ahmed, Rakesh Bhargava, Pandey DK & Sharma K: HIV infection sero prevalence in tuberculosis patients. **Ind J TB; 2003, 50, 151-154.**

15. Mohanty KC & Basheer PM: Changing trend of HIV infection and tuberculosis in a Bombay area since 1988; **Ind J TB 1995, 42, 117-20.**

16. Paranjape RS, Tripathy SP, Menon PA, Mehendale SM, Khatavkar P, Joshi DR, et al : Increasing trend of HIV sero prevalence among pulmonary tuberculosis patients in Pune, India; **Indian J Med Res 1997, 106, 207-211.**

17. Tripathy SP, Joshi DR, Menon P, Paranjape RS & Mehendale SM: Sero prevalence of HIV -1 infection in tuberculosis patients at Pune (abstract) X1, International conference on AIDS, Vancouver, Canada 1996.

18. Solomon S, Anuradha S & Rajasekaran: Trend of HIV infection in patients with pulmonary tuberculosis in south India; **Tuberc & Lung Dis 1995, 76, 17-19.**

19. Samuel NM, Alamelu C, Jagannath K & Rajan BP: Detection of HIV infection in pulmonary tuberculosis patients; **J Indian Med Assoc 1996, 94, 331-333.**

20. Talib SH, Bansal MP & Kamble MM: HIV-1 sero positivity in pulmonary tuberculosis; **Indian J Pathol Microbiol 1993, 36, 383-388.**

21. Banavalikar JN, Gupta R, Sharma DC, Goyal MK & Kumari S: HIV sero positivity in hospitalized pulmonary tuberculosis patients in Delhi; **Ind J TB 1999, 46, 17-20.**

22. Narain JP, Emanuele Pontali & Tripathy S: Epidemiology and control strategies. **Ind J TB, 2002, 49, 3-9.**

23. World Health Organization: A deadly partnership. Tuberculosis in the era of HIV. Global Tuberculosis Programme. World Health Organization publication (Geneva) **WHO/TB/96:204.**

24. Range N, Ipuge YA, Obrien Jr, Egeaga SM, Mfinanga SG, Conde TM, Mukadi YD & Borgdoff MW: Trend in HIV prevalence among tuberculosis patients in Tanzania 1991-1998; **AIDS 2001, 5, 401.**

25. Central TB Division, Directorate General of Health Services: Training manual for Medical Officers on HIV-AIDS Ministry of Health and Family Welfare, Nirman Bhavan, New Delhi.

26. Shafer RW, Small PM, Larkin C, Singh SP, Kelly P, Sierra MF, Schoolnik G & Chirgwin KD; Temporal trends and transmission pattern during the emergence of multidrug resistant tuberculosis in New York City: a molecular epidemiologic assessment; **J Infect Dis, 1995 Jan; 171, 170-6.**

27. National AIDS Control Organization and Central TB Division, New Delhi: Treatment guidelines for TB in HIV infected. Ministry of Health and Family Welfare, Government of India.

28. Central TB Division, Directorate General of Health Services, New Delhi: **TB India 2003. RNTCP status report.**