Current and future impact of HIV infection on tuberculosis morbidity (A case of Mumbai city in India)

by

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Abstract

Context

A combination of human immunodeficiency virus (HIV) and tuberculosis (TB) has transgressed all boundaries of the globe and it is now clear from the fact that the incidence of tuberculosis is increasing rapidly with the increasing pace of HIV epidemic. This rapid increase was highest in the last 10 years in India and affected mostly the sexually active population in the city of Mumbai (also known as the AIDS capital of India). Therefore, the assessment of the current and future impact of HIV on tuberculosis morbidity among sexually active population helps to have an appropriate plan for immediate control.

Methods

A case-control study has been done in Sir J.J. Hospital & Grant Medical College, Mumbai, to examine the impact of HIV on tuberculosis among sexually active age-group individuals (15-49 years). Odds ratio and population attributable risks were used as basic tools to assess the proportion of tuberculosis cases that are attributed to HIV among both HIV infected and overall population. To estimate the future impact of HIV on tuberculosis, the corresponding data are obtained from the Tuberculosis Control Programme (TCP), Brihanmumbai Municipal Corporation (BMC), Mumbai. A mathematical model has been used to predict the impact of HIV on tuberculosis, which describes and predicts the annual rates of breakdown of TB disease for any arbitrary population in the age-group of 15-49 years. The estimates were obtained under three different scenarios. The model equations are based on actuarial method and are developed recursively by Schulzer et.al. in 1994. The vital input of the model, incidence and prevalence rates of HIV was calculated using Epi-model package.

Results

The percentage of HIV sero positivity among tuberculosis patients increased significantly from 2.56 in 1988 to 22.7 in the year 1996 in Mumbai city. The results from a case-control study in the year 1996 reveal that the overall Mantel-Haenszel summary odds ratio for the impact of HIV on tuberculosis was found to be 3.1 (95% CI, 2.04 - 4.08). This ratio has been varied according to different socio-demographic characteristics of the patients. The results indicate that the proportion of tuberculosis cases that are attributed to HIV among HIV infected is 68 (95% CI, 50.9 – 75.4) per cent, and is 17 (95% CI, 12.8 – 19.1) per cent among the overall population. The results from the future impact of HIV on tuberculosis indicate that the intensity of increase in smear positivity rate increases with the increase in HIV incidence. The moderate scenario with HIV prevalence of 1.6% in the year 1998 would influx an estimate of increase at 129 per cent in smear positivity rates in the year 2000 relative to the pre-HIV year 1985 and the corresponding increase for the year 2005 is estimated at 278 per cent.

Conclusion

One sixth of total tuberculosis cases in the age-group of 15-49 years are attributed to HIV in the population currently, and the burden will increase by almost 3 fold by the year 2005 relative to the pre-HIV year 1985 with a dramatic increase in HIV associated sputum positive tuberculosis cases. In HIV, prevention is the cure, but in tuberculosis both prevention and cure are important. Curing more number of infectious (sputum positive) tuberculosis cases itself prevents the transmission of the disease. And, it is equally important to take steps or explain the care for prevention of tuberculosis in the population.

Key Words: HIV, AIDS, TB, ELISA, incidence, prevalence, smear positivity, odds ratio (OR), attributable risk (AR)

Introduction

To make the global situation worse, tuberculosis has formed a lethal combination with HIV, the AIDS virus each speeding the other's progress.[1] Clinical and surveillance studies show that tuberculosis is the most important life threatening and opportunistic infection amongst people with compromised resistance as a result of HIV infection.[2-4] Tuberculosis was already a serious public health problem in India with 1.5 million new cases being reported annually and that the country responsible for fifty percent of incidence world wide.[5-8] Currently, 14 million people are estimated to be suffering from active tuberculosis in India of which 3 to 3.5 million are highly infectious sputum positive cases.[6,9] The rate of tuberculosis in 1991 has been the highest since independence which is a cause for concern keeping in view the onslaught of AIDS in the country and the likelihood of further increase of the disease.[10] The pandemic of infection with human immunodeficiency virus (HIV) seems to have a profound medical, social and economic impact, particularly in India, when a gradual-declining trend of reported tuberculosis cases up to 1988 was reversed.

Mumbai, the capital of Maharashtra state is one of the most populated cities in India.[11] Tuberculosis morbidity situation in Mumbai city is no different from India. There was a declining trend of tuberculosis incidence in the city from 1982 (the year Short Course Chemotherapy Treatment was introduced) to 1990; but after 1990, there has been a rapid increase in the reported cases of tuberculosis especially in the young ages (Unpublished data, TB Control Programme, BMC). It is stated that, Mumbai is the frontier of a devastating combination: a huge population, high incidence of tuberculosis and a fast emerging epidemic of HIV.[12] The serious danger signals of HIV were felt but hardly any attempt has been made to study the impact of HIV on tuberculosis even in India. Keeping this in view, an attempt has been made in this paper to study the trends of HIV associated tuberculosis and estimate the impact of HIV on tuberculosis. For careful planning of the health system to control the rapid tuberculosis increase in the city, estimates on current and future impact of HIV on

Several models were developed to study the epidemiology of tuberculosis in the past.[13-16] All these models were dependent on single epidemic disease and fail to account the behaviour of two epidemic diseases. For diseases like HIV and tuberculosis, where the large number of susceptible and greater associations are present in the population, the models developed generally on the spread of epidemics can not be used. Hence, a recently developed mathematical model[17] which documents the interaction of HIV and TB has been used in this paper to predict the impact of HIV on tuberculosis incidence anticipated for the present decade so that health care can be carefully planned, sufficiently funded and effectively implemented.

Methods

To estimate the current impact of HIV on tuberculosis, a case-control study was conducted in a hospital in the city of Mumbai, one of the largest cities[11] located in the central part of India. Study was conducted in Sir J.J.Hospital, a tertiary service centre with modern medical technology and is one of the well-known hospitals of the city. Patients from all the areas use the services of this hospital and it is the first to start HIV surveillance centre in the city in the year 1987. Since then, all the tuberculosis in-patients of the hospital were tested for HIV and the same data has been used in the present paper to study the trends of HIV associated tuberculosis morbidity.

To a case-control study, Cases were defined as the patients with confirmed tuberculosis, who had been identified at the TB clinic, Sir J.J. Hospital between 1st January and 31st December, 1996. Repeated smear examination and x-ray findings were used to consider the confirmed cases of tuberculosis in the study. The controls were identified from the patients attending HIV surveillance centre of the same hospital, with similar characteristics such as age, gender and exposure to HIV but of non-tuberculosis disease. The control subjects were mostly the patients with diagnosis to gastroentiritis, malarial fever, and acute liver disease due to alcohol consumption.

A rough estimate of twenty five percent of HIV infections among tuberculosis patients of sexually active age-groups (15-49 years) with a desirable precision of 5 per cent indicates a sample size of 323 subjects in both cases and controls.[18] To achieve this, the relevant data are obtained from 470 cases and 357 control subjects. Patients below 15 and above 50 years of age are ignored assuming a negligible proportion of HIV associated tuberculosis diseases in them. Information on socio-demographic characteristics and history of HIV was collected from all the subjects participated in the study using a standard questionnaire. Enzyme Linked Immunosorbent Assay (ELISA) test was used for HIV examination. The cases and control subjects were matched according to age and gender for the purpose of statistical analysis. Calculation of odds ratio and attributable risks were employed to examine the impact of HIV on tuberculosis. Mantel-Haenszel summary odds ratio[19] was calculated to eliminate the bias effects on the estimates. The detailed methodology is shown in Appendix-A.

To estimate the future impact of HIV on tuberculosis, a mathematical model has been used, which describes and predicts the annual rates of breakdown of TB disease for any arbitrary 15-49 year old population subjected to both TB and HIV infections. Beginning with the year in which HIV infection was probably first present in the population, the model calculates the growing yearly incidence rates of new TB disease in HIV-positive and HIV-negative individuals. Model equations are derived from an actuarial method, are developed recursively. The detailed methodology of the model was given elsewhere.[17]

The final model equations are given as:

$$NN_t = (1-ß_1)(1-Q_t).[(1-P_0)R_0\sum_{l=1}^{7}A_l(\sum_{i=1}^{5l+12}p_{i,5l+12}) + \sum_{i=t}^{t-1}(1-P_{t-i})R_{t-i}(\sum_{l=1}^{7}A_l p_{i,5l+12})]$$

and

$$PN_t = \frac{ß_1}{1-ß_1}NN_t$$

Further, one obtains:

$$NP_t = (1-ß_2)\sum_{j=1}^{t}(1-Q_{t-j})q_{t-j}(1-\sum_{s=1}^{j}d_s).[(1-P_0)R_0\sum_{l=1}^{7}A_l(\sum_{i=1}^{5l+12}p_{i,\,j,5l+12})$$

$$+\sum_{i=1}^{t-i}(1-P_{t-i})R_{t-i}(\sum_{l=1}^{7}A_l p_{i,\,j,5l+12})]$$

and

where,

$$PP_t = \frac{ß_2}{1-ß_2}NP_t$$

NN_t, PN_t, NP_t, PP_t, respectively the rates of incidence of TB disease in year t, (t>0), for: smear-negative/HIV-negative (NN_t), smear-positive/HIV-negative (PN_t), smear-negative/HIV-positive (NP_t), and smear-positive/HIV-positive (PP_t) cases.

$ß_1$: the proportion of new HIV-negative TB disease cases who are smear-positive.

$ß_2$: proportion of new HIV-positive TB disease cases who are smear-positive.

P_0: Constant pre-HIV annual prevalence rate of TB infection.

R_0: constant pre-HIV annual prevalence rate of TB infection.

P_t: annual prevalence rate of TB infection in year t of the HIV infection.

Q_t: annual prevalence rates of HIV infection in study population in year t.

R_t: annual risk of TB infection in year t of the HIV infection.

p_{ik}: probability that an individual who became infected with TB at age k-i ($k \geq i$) will break down with TB disease at age k years (i.e. i years after becoming infected with TB) and not before ($p_{0k}=0$);

$q_{t:}$ annual incidence rates of HIV infection in study population in years t = 0,1,2,…. of the HIV infection; d_s: probability of dying 1,2,3,….. years after becoming infected with HIV; A_l: proportion aged in different age-groups.

The input information required for the application of this model are: population distribution, prevalence of tuberculosis, and smear positivity rates - at the start of the HIV year in the city or country; HIV incidence and prevalence rates over the years from the start of the HIV era; annual breakdown rates of tuberculosis among HIV- positive and negative individuals; and annual TB death rates. The population distribution (pre-HIV era) in different age-groups were calculated using the exponential growth rate method. The growth rate was estimated using the inter-censal population of Mumbai city.[20] The annual incidence and prevalence rates of HIV were estimated by using the Epi-model computer package.[21] The information provided for the application of the package are: start of the year of HIV, Prevalence rate of HIV in the reference year and the rate of inflation (either exponential or gamma distribution). In this paper, the start of the HIV era was considered as 1985 and the

prevalence of HIV in the year 1998 was assumed to be between 1.2 and 2 per cent. The inflation rate of HIV was assumed to follow Gamma distribution due to its constant rate of HIV incidence in the population over the years from 1995 to 1998 although it does not decline.[22] However, its effect on the prevalence cases do not have impact, as the infected cases continue to detect in the recent years when they progress to AIDS or get in contact with the opportunistic infections more commonly the tuberculosis.

Information on breakdown rates of tuberculosis among both HIV positive and negative individuals were obtained from the literature, observed data, and experts opinions [breakdown rates of tuberculosis among dually (HIV+TB) infected individuals]. Data on tuberculosis death rates were obtained from the reports of TCP, Mumbai. Relatively the model equations are derived and the results are presented for annual incidence and prevalence rates of tuberculosis infection as per the input data.

Results

Trends of HIV seropositivity among TB patients

The results in table 1 shows the number of patients screened each year, the number reactive in ELISA for HIV and the number confirmed positive in both males and females. A total of 5324 patients were admitted for various respiratory ailments to TB Clinic of Sir J.J.Hospital, Mumbai during 1988-96. Of which, 520 patients (9.8 per cent) were found HIV positive by the ELISA test. About ninety eight per cent of HIV associated tuberculosis patients are in the age-group of 15-49 years. The proportion of TB patients with HIV showed a significant increase over the years from 2.56 per cent in 1988 to 22.7 per cent in the year 1996.

It was evident from the results that the proportions of HIV infected among tuberculosis patients were slightly higher for males compared to females, however the difference was insignificant. Among males, 2.67 per cent of tuberculosis patients are with HIV in the year 1988, and this proportion has relatively increased to 23.1 per cent by the year

1996. For females, it was 2.13 per cent in the year 1988 and increased to 21.4 per cent in the year 1996. The increase in the proportion of HIV among male tuberculosis patients had odds of 8.64 times higher in the year 1996 as compared to the year 1988, while for females the odds were ten times higher in the year 1996 as compared to the year 1988. The increasing prevalence of HIV among tuberculosis patients indicates that HIV has a significant influence on the incidence of tuberculosis in the city.

Current Impact of HIV on tuberculosis

Percentage distribution of HIV among selected cases and controls

Proportion of HIV infections was high at 25 per cent among tuberculosis cases and 10 per cent among the control subjects in the year 1996 (Table 2). Major concentration of infection in both the subjects (cases and controls) were observed in the age of 25-44 years. While the HIV infection among tuberculosis was more for males compared to females in TB cases and vice-versa in control subjects, however, the difference is not statistically significant.

Impact of HIV on tuberculosis

The results in table 3 revealed that the overall Mantel-Haenszel summary odds ratio for the development of tuberculosis was 3.1 (95% CI, 2.04 - 4.08) with the exposure to HIV. The higher odds ratio found for the 25-34 year age group (4.52, 95% CI 2.48 – 8.49) and lower odds for those aged above 45 years (1.38, 95% CI 0.44 – 5.20). Further, an odds of HIV infection for the development of tuberculosis was 5.14 (95% CI, 2.39 – 12.66) among males, whereas for females it was only 2.14 (95% CI, 1.17 – 3.92).

The odds of HIV infection on tuberculosis among hindu patients was high at 3.81 (95% CI, 2.35 – 6.33) compared to only 1.34 (95% CI, 0.58 – 3.26) among non-Hindus. No significant association found between income and the impact of HIV on tuberculosis. This clearly indicates that the development of active tuberculosis due to HIV infection is more or less similar for all the income categories. While doing the case-control studies to examine the impact of specific exposure on disease, it would interest to know the risk of prevalence of

disease attributed to specific exposure, which gives a useful information among both the exposure group and the overall population.

Attributable risk

Among HIV infected

The odds ratio was used further to calculate the proportion of TB cases that are attributed to HIV among HIV infected. In all, 68 (95% CI, 50.9 – 75.4) per cent of tuberculosis cases were attributed to HIV among HIV infected in the year 1996 (Table 3). The percentage of tuberculosis cases that are attributed to HIV in the age-group of 25-34 years was highest at 78 and the corresponding percentages for other age-groups such as 15-24, 35-44 and 45+ years were 68.5, 54 and 27.5.

Four-fifth of the male tuberculosis patients were attributed to HIV and in case of females it was 53 per cent. Majority of the females infected to HIV were the commercial sex workers.[23] These sex workers claim that economic imbalances in the family are the main reasons forcing to choose sex as profession (Unpublished data). After the detection of HIV either accidentally or due to other opportunistic infections, they are treated differently by both family and the society force them to be at higher risk for activation and progression of the TB bacilli.[23] Literally quoted this as, "the women are however often seen as the transmitters of HIV in the society -- as a sex worker who spreads the virus or as a mother who gives the virus to her unborn child".[24] Though, the women are transmitters, males are carriers of this infection to their wives and other women.[24]

Among the overall population

The last column in Table 3 indicate that 17 (95% CI, 12.8 – 19.1) per cent of tuberculosis cases in general among the sexually active age-group individuals were attributed to HIV infection. This fraction found to be high in the age-group of 25-34 years at 30 per cent and was relatively low for the ages 45 and above at 3.5 per cent. It suggests that the attributable risk of HIV associated tuberculosis was highest among the young middle age-group and this proportion

Risk of tuberculosis due to HIV among males and females was 20.9 and 12.5 per cent respectively. Among Hindus, the proportion of tuberculosis attributed to HIV was 21 per cent, whereas the corresponding percentage for non-Hindus was only four. The reasons for significant differences between Hindus and Non-Hindus in terms of tuberculosis morbidity were yet to be known clearly. Level of income has a negative association with the attributable risk in this situation show a lower risk among the higher income people prompts that, sufficient level of nutrition helps the inactivation of bacilli. It indicates that nutritional intake has a vital part to play in the activation of bacilli irrespective of exposure to HIV.

Future impact of HIV on Tuberculosis

Exponential growth rate method was used to estimate the population in different age-groups in the year 1985 (Table 4). Using the population in different age-groups, the distributions of the population have been tabulated. The distribution of the population was found to be more or less uniform across different age groups in the city of Mumbai among 15-49 year age individuals.

Estimated Incidence and Prevalence rates of HIV

The prevalence of HIV infection in Mumbai city was estimated as 1.6 per cent in the year 1998 (DHS, Maharashtra). Not to be too conservative with the available estimate of the prevalence of HIV, it was assumed that the range of HIV prevalence may vary between 1.2 and 2 per cent. Further, the incidence rates of HIV are assumed to decline over the years after 1998, although many researchers contradict this. A unit fall in HIV prevalence from 1993 (1.7 per cent) to 1998 (1.6 per cent) (DHS, Maharashtra) allows and initiate the assumption. However, the prevalence rates of HIV infections do not decline as the average survival of HIV/AIDS was assumed to be seven years. Therefore, the prevalence number of HIV infections continues to increase in the population even if the incidence rate declines. The incidence rates of HIV in the year 1994 are estimated to be 174, 238 and 299 respectively per 100,000 population decline to 110, 108 and 204 by the year 2004 provided

at different prevalence rates of HIV in the year 1998. However, the prevalence rates of HIV in the year 1998 continue to increase from 1200, 1599 and 2056 respectively to 1431, 1655 and 2464 by the year 2004. These rates are the estimates of HIV incidence and prevalence at low, medium and high risk scenarios (Table 5).

TB disease breakdown rates among HIV positive and negative individuals

The estimated risk of tuberculosis annually in persons with HIV and tuberculosis co-infection is 5-10 per cent, with a lifetime risk as high as 50 per cent or greater.[26] In the present conditions, the lifetime risk of developing tuberculosis among dually infected is considered to be fifty per cent (Table 6) with different probabilities each year (p_{ijk}, $i \geq j$). The underlying probabilities of risk of developing tuberculosis from the time of infection to HIV are smoothed accordingly with the assumption of eight per cent per year. Further, the development of tuberculosis among HIV infected individuals after the year of infection was 80 per cent as the estimates show, between 60-80 per cent of AIDS cases develop tuberculosis.[6]

Among the non-HIV individuals, lifetime risk of developing tuberculosis is taken as 10 per cent. The HIV mortality rates according to the duration of infection are accelerated and smoothed averaging 7 years of survival. Further, it is assumed that by the end of 11^{th} year, all the individuals having HIV infection surely die of either tuberculosis or any other HIV associated ailments. The annual mortality rates following HIV infection were shown in table 6.

Predicted incidence rates of smear-positivity

The estimates for the future impact of HIV on tuberculosis were made under three scenarios. The Low burden (scenario I) indicates the annual risk of TB infection in the year 1986 with 2 per cent, and HIV prevalence of 1.2 per cent in the year 1998 (MDACS, 1998[25]; DHS, Maharashtra, unpublished data). The Moderate burden (scenario II) indicates the annual risk of TB infection of 2 per cent in the year 1986, and HIV prevalence of 1.6 per cent (among blood donors) in the year 1998 (DHS, Maharashtra, unpublished data). The High burden (scenario III) indicates the annual risk of tuberculosis infection of 2 per cent in

the year 1986, and HIV prevalence of 2 per cent in the year 1998 (DHS, Maharashtra, unpublished data).

The results of the model indicates that the per cent increase in smear positivity rates in the year 2000 relative to the pre-HIV year 1985 is estimated at 70 per cent and the increase in the year 2005 relative to pre-HIV year 1985 is estimated at 178 per cent under the low risk of HIV (Table 7). Further the increase in smear positivity rates in the years 2000 and 2005 relative to the pre-HIV year 1985 are estimated at 129 per cent and 278 per cent respectively under the medium risk scenario. The 2 per cent prevalence of HIV in the year 1998 shows an abnormal in crease in smear positivity rates in the years 2000 and 2005 are estimated at 154 per cent and 416 per cent respectively relative to the pre-HIV year 1985. It is noticed that the estimates on smear positivity rates obtained under the moderate scenario were found closer to the figures observed on smear positive tuberculosis cases among the sexually active age individuals in the city (Unpublished data, TCP, Mumbai).

Discussion

The present study summarises the impact of HIV on tuberculosis in the past, current and for the future in the city of Mumbai. Mumbai city is known as the capital of Maharashtra state geographically and AIDS capital of India epidemiologically. It became a largely populated city in the year 1998 with 1.12 crore inhabitants. Migration into the city was highly responsible for increase in its population size. The estimated mid-year population in the year 1996 was 1.09 crores,[11] of which, more than half (52 per cent) are in the age group of 15-49 years. The first HIV associated tuberculosis case in India was detected in the year 1987 in Sir J.J.Hospital, Mumbai.[27] In continuation, the results indicate a ten-fold increase in the proportion of HIV seropositivity among tuberculosis patients over the years from 1988 (2.56 per cent) to 1996 (22.7 per cent). These results are supported by a study in Pune (a city closer to Mumbai) revealed that the overall seroprevalence of HIV among newly diagnosed tuberculosis patients [illegible] [28] M[illegible]

HIV's seropositivity has raised from 2.5 per 1,000 to an official 22 per 1,000 across the board.[29] Add to this the warning that one out of every five Indians is an adolescent (between 15-24 years), and this is the most vulnerable group on these sexually driven disease counts.

The prevalence of HIV was found significantly higher among the younger age-groups and among the low income categories. The risk of tuberculosis due to HIV was found to be high in the age-group of 25-34 years, and the reasons of this were probably attributed to the high risk behaviours. Among the HIV infected adults, tuberculosis is one of the most common opportunistic diseases.[30,31] HIV infected individuals have 5-10 per cent annual risk of developing tuberculosis[31,32] and an estimated life-time risk of developing clinical tuberculosis of 30 per cent or more among the young adults.[31,33] These were evident from the recent rapid increase in the incidence of tuberculosis, coincident with the spread of the HIV epidemic in the adult populations.

The overall Mantel-Haenszel summary odds ratio for the impact of HIV on tuberculosis was found to be 3.1 (95% CI, 2.04 - 4.08). The odds ratios obtained in this study are quite similar with the findings obtained world over. Due to lack of case-control studies with this objective in India, the results were compared with the results of other developing countries. In Uganda during the period 1990-92, the relative risk for HIV infection among patients with tuberculosis in four sentinel hospitals compared to women attending antenatal clinics at the same hospitals was 5.9 (95% CI, 5.1 - 6.9).[34] In Tanzania, HIV seroprevalence was 29 per cent in 1991-92 among patients with tuberculosis, and the odds ratio for HIV infection was 5.4 for patients with sputum smear-positive tuberculosis, when blood donors were used as controls.[35] A study in Abidjan, Ivory Coast, revealed that the odds ratio associated with HIV-1 infection was 4.7 (95% CI : 3.6-6.2).[36] A population based study in Malawi revealed an odds ratio of 7.4 (95% CI: 3.3-16.7) associated with HIV infection for those having tuberculosis.[37] A study in Tanzania concluded that HIV seropositivity in TB patients has a mean 3.5 times higher than in the general population.[38]

The younger age and male population are at higher risk of contracting tuberculosis because of HIV. The highest risk (OR 4.52, 95% CI 2.48 – 8.49) were noticed in the age-group of 25-34 years and the lowest risk (OR 1.38, 95% CI 0-44 – 5.20) were noticed among the age-group of 45-59 years. The results of this analysis were quite similar with the findings of the studies world over. In a study in Tanzania, the odds ratio is highest with 13.4 (95% CI, 8.9 – 20.7) for the age-group 25-34 years, and the lowest of 2.9 for the age-group 45-54 years.[3] Similar findings but with different magnitudes of odds ratios were observed in many studies.[39,40] The variation of this risk seen between different studies mainly due to the selection bias in defining control subjects and lack of adjustment for confounding. However, it is a fact that HIV infection greatly increases the risk of active tuberculosis in those who have been newly infected with tuberculosis bacilli.[41,42] Proven the fact that young age individuals are at high risk for HIV associated tuberculosis. Comparatively males have higher odds than females may be due to the frequent exposure to TB bacilli by males outside in the society. Even otherwise, male tuberculosis cases outnumber female tuberculosis cases in terms of morbidity.

The proportion of tuberculosis cases that are attributed to HIV among HIV infected was 68 (95% CI, 50.9 – 75.4) per cent in Mumbai city. **This finding has gained importance especially when there was no evidence of statistical data to show between 60 to 80 per cent of HIV/AIDS cases develop tuberculosis in India.** According to the studies world over and Delphi's technique in India, more than 60 per cent of HIV/AIDS cases have developed tuberculosis.[6,43] The National AIDS Control Organisation (1993) reports by the end of year 1993, of the 559 AIDS patients, 331 (60 per cent) had evidence of active tuberculosis.[44] It also reports that in India currently there are about 0.75 million persons infected by HIV. Assuming that half of these are infected with tuberculosis, the breakdown rate from TB infection to disease among dually infected individual is 10% per year than more than 35000 HIV related TB cases are likely to occur annually in India.[44] Males are at higher risk of getting HIV associated tuberculosis complications among HIV infected than their female counterparts.

Similar are the findings even among the general population according to age, sex, income and religion of the patients.

The above findings indicate that HIV is the most potent factor for increase in tuberculosis morbidity in Mumbai city. Therefore, an attempt has been made to apply a mathematical model to predict the impact of HIV on Tuberculosis in the future for the public health planning. The advantage of this model mainly provides a useful blueprint for health agencies in designing effective programme for curbing the future course and development of these devastating dual epidemics in the community. It estimates the future impact of HIV on tuberculosis and the model is flexible enough to fit the current data in India for the estimation. The model calculates the incidence of smear positivity (infectious) rates among both HIV positive and negative individuals from the start date of HIV infection to 20 years long. As of now, the tuberculosis has become a great problem in public health and shows a danger mark even for the future. For illustration, the increase in smear positivity rates in the years 2000 and 2005 relative to the pre-HIV year 1985 are estimated to be in the ranges of 1.7 to 2.8 times and 2.5 to 5.5 times respectively. These findings suggests that the increase in smear positivity rates because of the increase in HIV infections or its impact within the twenty years of the start of HIV infection in the population is considerably significant.

Conclusively, the findings suggests that more than one-sixth of the tuberculosis patients in the general population among 15-49 age-group individuals are attributed to HIV and more specifically males and of younger age populations are at higher risk of dual infection. Continued the increasing trends of tuberculosis morbidity associated with HIV, the overall smear positivity rates are going to increase dramatically to a maximum of 5 times by the year 2005 compared to the start of the HIV year 1985. Keeping these findings in view it is suggested that there should be a fight to combat with both HIV/AIDS and tuberculosis. The cure and decline in the incidence of tuberculosis is possible even among the HIV patients with the help of Short Course Chemotherapy under DOTS strategy, therefore efforts should be

proper awareness programmes. As prevention is the most important feature for fight against HIV/AIDS and, both prevention and cure are the important features to fight against tuberculosis. The public health interventions should concentrate to cure more number of sputum positive cases of tuberculosis at clinical side. On the other hand, efforts have to be made to increase the health awareness and the available facilities against deadly infections.

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Appendix - A

The odds ratio (OR) will provide an estimate of the relative risk of tuberculosis for HIV-infected persons compared to non-infected. And attributable risk was defined as the proportion of disease incidence (or disease risk) which can be attributed to a specific exposure. Thus, attributable risk was used in the present study to estimate the proportion of tuberculosis cases that can be attributed to HIV, both in the exposed (HIV-infected) and overall population.

In notations, the odds ratio is given as

$$OR = (ad) / (bc)$$

OR is then used to calculate the attributable risk as follows:

1. To determine the proportion of tuberculosis cases attributable to HIV infection among the HIV infected:

$$1 - 1/OR$$

2. To determine the proportion of tuberculosis cases attributable to HIV infection among the overall population, the following formula has been used.

$$(1-1/OR) * (a/a+c)$$

where $a/a+c$ is the prevalence of HIV infection among TB patients

If data are available by age and sex in both cases and controls, it is better to estimate the OR from stratified data using the Mantel-Haenszel summary estimate:

	TB cases	Controls	Total
HIV (+)	a_i	b_i	n_1
HIV (-)	c_i	d_i	n_2
Total	m_1	m_2	T_i

$$\text{Summary odds ratio} = \sum(a_i.d_i/T_i) / \sum(b_i.c_i/T_i)$$

Table 1 Trends of HIV seropositivity among TB patients in Mumbai city, 1988-96

Year	Total TB patients			Prop. Of HIV among TB			Odds ratio†		
	M	F	Total	M	F	Total	M	F	Total
1988	374	94	468	10 (2.67)	2 (2.13)	12 (2.56)	1.00	1.00	1.00
1989	505	202	707	14 (2.77)	5 (2.48)	19 (2.68)	1.04	1.16	1.04
1990	453	188	641	19 (4.20)	6 (3.20)	25 (3.90)	1.57	1.50	1.52
1991	527	151	678	51 (9.68)	14 (9.27)	65 (9.59)	3.62	4.36	3.73
1992	481	115	596	48 (9.98)	11 (9.56)	59 (9.90)	3.73	4.49	3.86
1993	594	194	788	61 (10.27)	19 (9.80)	80 (10.15)	3.84	4.60	3.95
1994	354	108	462	48 (13.56)	12 (11.10)	60 (12.98)	5.07	5.22	5.06
1995	332	120	455	65 (19.70)	15 (11.70)	80 (17.50)	7.37	5.87	6.85
1996	389	140	529	90 (23.10)	30 (21.40)	120 (22.70)	8.64	10.07	8.84
Total	4009	1312	5324	406 (10.1)	114 (8.7)	520 (9.8)			

Note: M - Males, F - Females

† The year 1988 was considered as base year for the calculation of odds ratio

Data Source: TB Clinic and HIV Surveillance Centre, Sir J.J.Hospital & Grant Medical College, Mumbai.

Table 2 HIV prevalence in cases and controls according to different background characteristics, 1996

Characteristics	Cases‡		Controls$	
	% infected	Number of subjects	% infected	Number of subjects
Age-group				
15-24	16.3	80	5.7	87
25-34	38.9	167	12.3	154
35-44	23.7	114	12.5	64
45-49	12.8	109	9.6	52
Sex				
Males	26.0	342	6.4	125
Females	23.4	128	12.5	232
Religion				
Hindus	28.7	338	9.6	272
Non-Hindus	16.7	132	12.9	85
Income				
No income	26.2	336	11.8	212
Less than 1000	26.2	107	9.9	101
1000+ more	11.1	27	4.5	44
Total	25.3	470	10.4	357

‡ Bacteriologically confirmed cases of tuberculosis (patients with TB bacilli)

$ Patients attending HIV Surveillance centre of Sir J.J.Hospital with non-tuberculosis ailments and tested for HIV

Data Source: TB Clinic and HIV Surveillance Centre (for cases) & Dept. of Medicine (for control subjects), Sir J.J.Hospital & Grant Medical College, Mumbai.

Table 3 Impact of HIV on Tuberculosis according to different background characteristics, 1996

Characteristics	Odds ratio	Attributable Risk	
		Prop. of TB cases attributable to HIV infection among HIV infected (%)	Prop. of TB cases attributable to HIV infection among over all population (%)
Age-group			
15-24	3.18 (1.00 – 11.9)	68.5	11.1
25-34	4.52 (2.48 – 8.49)	77.8	30.0
35-44	2.17 (0.88 – 5.91)	53.9	12.7
45-49	1.38 (0.44 – 5.20)	27.5	3.5
Sex			
Males	5.14 (2.39 – 12.6)	80.6	20.9
Females	2.14 (1.17 – 3.92)	53.3	12.5
Religion			
Hindus	3.81 (2.35 – 6.33)	73.7	21.2
Non-Hindus	1.34 (0.58 – 3.26)	25.4	4.2
Income			
No income	2.65 (1.61 – 4.49)	62.3	16.3
less than 1000	3.23 (1.41 – 7.89)	69.0	18.1
1000+ more	2.62 (0.28 – 33.0)	61.8	6.9
Total	**3.10♣ (2.04 – 4.08)**	**67.8 (50.9 – 75.4)**	**17.2 (12.8 – 19.1)**

♣ Summary estimate obtained from Mantel-Haenszel odds ratio

Table 4 Age distribution of population in Mumbai city, 1985

Group	Mean Age	Proportion (%)
1	17 (15-19)	16.36
2	22 (20-24)	18.84
3	27 (25-29)	17.85
4	32 (30-34)	14.94
5	37 (35-39)	13.42
6	42 (40-44)	10.26
7	47 (45-49)	8.31
1-7	15-49	100.00

Data Source: Census of Maharashtra, 1981 and 1991 data

Table 5 Annual Estimated incidence and prevalence rates[‡] corresponding to the prevalence of different scenarios of HIV infection

Year	1.2% of HIV prevalence in the year 1998		1.6% of HIV prevalence in the year 1998		2% of HIV prevalence in the year 1998	
	Incidence	Prevalence	Incidence	Prevalence	Incidence	Prevalence
1985	0	0	0	0	0	0
1986	1	0	1	1	1	1
1987	13	14	25	26	23	24
1988	34	48	61	86	60	83
1989	62	109	105	188	107	187
1990	92	197	148	330	158	338
1991	120	302	186	502	206	529
1992	144	438	214	690	247	751
1993	162	576	231	883	279	988
1994	174	717	238	1066	299	1229
1995	181	851	237	1232	310	1460
1996	182	974	228	1371	312	1671
1997	181	1095	217	1500	310	1878
1998	176	1200	202	1599	302	2056
1999	168	1285	185	1669	289	2203
2000	157	1350	167	1711	271	2315
2001	147	1396	149	1725	252	2393
2002	135	1422	132	1715	231	2438
2003	122	1430	114	1684	210	2452
2004	110	1431	108	1655	204	2464

‡ per 100 000 population

Table 6 TB disease breakdown rates (in % per year) and mortality rates of HIV in adults of 15-49 age-group

TB Disease Breakdown rates				Duration (in yrs.)	HIV mortality rates
P_{ik}	p_{ijk}				
	i<j i=1,2,……,10		i≥j j=1,2,….,10		
i= 1 5.0	1	42.1	1 8.0	1	0
2 2.0	2	16.8	2 7.4	2	0
3 0.5	3	4.2	3 6.8	3	5
4 0.5	4	4.2	4 6.2	4	5
5 0.5	5	4.2	5 5.7	5	10
6 0.2	6	1.7	6 5.3	6	10
7 0.2	7	1.7	7 4.8	7	20
8 0.2	8	1.7	8 4.4	8	20
9 0.2	9	1.7	9 1.1	9	20
10 0.2	10	1.7	10 0.3	10	5
≥11 0.1				11	5

p_{ik} rates for HIV-negative individuals aged k years, infected with TB i years ago. The p_{ik} in this exercise were assumed to be independent of age k, depending only on I, the number of years since TB infection.

p_{ijk} rates for HIV-positive individuals aged k years, infected with TB i years ago and with HIV j years ago.

i<j TB infection following HIV infection. Breakdown rates were assumed to be proportional to those of HIV-negative adults, but were scaled up to total 80% breakdown in the first 10 years after TB infection. Rates for i >= 11 were not defined, due to the HIV mortality rates assumed shown in the last column of the above table.

i ≥ j TB infection prior to HIV infection. Breakdown rates were assumed to be 8 per cent life time risk averaging to a total of 50% in 10 years. Rates for j >= 11 were not defined, due to the HIV mortality rates assumed.

Table: 7 Predicted incidence rates (per 100 000) of smear-positive TB cases in 15-49 age-group, under three scenarios of HIV burden

Year	Scenario I		Scenario II		Scenario III	
	HIV -ve	HIV +ve	HIV -ve	HIV +ve	HIV -ve	HIV +ve
1985	37	-	37	-	37	-
1986	37	0	37	0	37	0
1987	37	0	37	0	37	0
1988	37	0	37	0	37	0
1989	36	0	36	0	36	0
1990	36	0	36	0	36	0
1991	35	0	35	0	35	0
1992	35	0	35	1	35	1
1993	34	1	34	2	34	2
1994	34	2	34	4	34	4
1995	34	4	34	7	34	7
1996	34	6	35	11	35	12
1997	35	10	36	16	36	18
1998	36	14	38	23	39	26
1999	37	18	42	31	42	36
2000	40	23	46	39	47	47
2001	43	28	51	47	53	60
2002	46	33	57	54	61	73
2003	51	37	63	60	69	86
2004	55	41	69	64	78	97
2005	59	44	75	65	85	106

Note: Estimates with R_0 = 2% (pre-HIV annual risk of TB infection), P_0 = 60% (pre-HIV annual prevalence of TB infection, Q_{14} = Under different scenarios (HIV infection prevalence in year 1998)

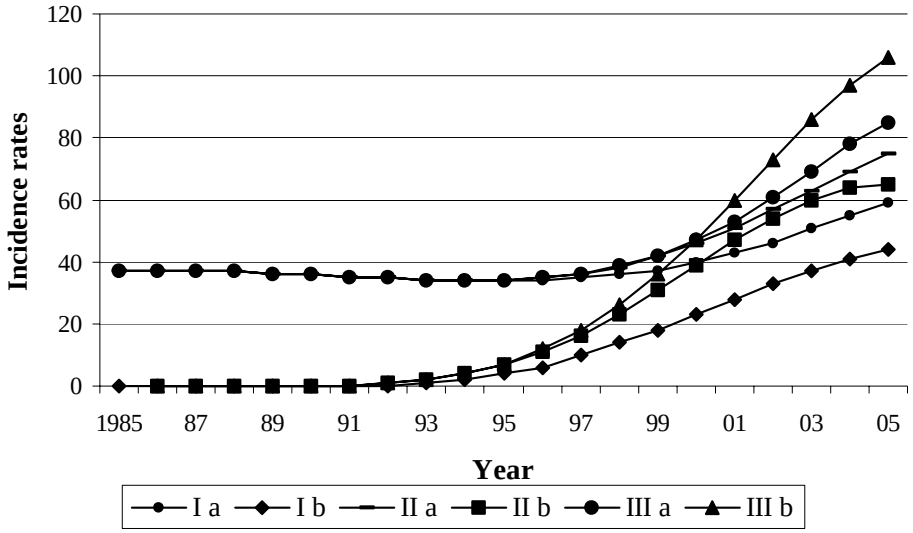
Scenario I – HIV prevalence of 1.2 per cent in the year 1998

Scenario II – HIV prevalence of 1.6 per cent in the year 1998

Scenario III – HIV prevalence of 2 per cent in the year 1998

Figure 1

Smear-positivity rates (per 100,000 population) among HIV positive and negative individuals for the prevalence of different estimates of HIV in the year 1998



Ia - Incidence rate among HIV negative tuberculosis individuals at 1.2% prevalence in the year 1998
Ib - Incidence rate among HIV positive tuberculosis individuals at 1.2% prevalence in the year 1998
IIa - Incidence rate among HIV negative tuberculosis individuals at 1.6% prevalence in the year 1998
IIb - Incidence rate among HIV positive tuberculosis individuals at 1.6% prevalence in the year 1998
IIIa - Incidence rate among HIV negative tuberculosis individuals at 2% prevalence in the year 1998
IIIb - Incidence rate among HIV positive tuberculosis individuals at 2% prevalence in the year 1998