

THE INCIDENCE OF TUBERCULOSIS IN HIV INFECTED PATIENTS IN A TERTIARY CARE CENTRE OF KOPPAL DISTRICT

Krishnakumar Naik¹, Srinivas Jutur², Shivaprasad T¹, Umesh Rajoor³, Gavishiddesh Vishwanath Ronad⁴

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Corresponding Author:
Dr. Gavishiddesh Vishwanath Ronad,
Email: prasangavi@gmail.com
ORCID: 0000-0001-8279-4403

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¹Assistant Professor, Department of General Medicine, KIMS, Koppal, Karnataka, India

²Associate Professor, Department of General Medicine, KIMS, Koppal, Karnataka, India

³Professor, Department of General Medicine, KIMS, Koppal, Karnataka, India

⁴Senior Resident, Department of General Medicine, KIMS, Koppal, Karnataka, India

Abstract

Background: Tuberculosis disease (TB) has surpassed HIV as the leading infectious cause of mortality globally. The objectives is to know the incidence of tuberculosis in HIV infected patients in a tertiary care centre of Koppal district. **Materials and Methods:** We conducted a retrospective cohort study of HIV-infected adults registered at the District Hospital ART center in Koppal, India. All patients registered at the ART center received free clinical care and treatment as per national program guidelines. **Result:** Total 3762 HIV patients are under follow up in our ART centre among them 88(n) patients were newly detected with tuberculosis by CBNAAT and were started on Anti tubercular therapy. Among total HIV patients 88 patients were diseased with tuberculosis also in one year. among 88 patients 52 patients were of the age ≤40 years and 36 patients were of the age > 40 year. Among total patients 49 were males and 39 were females. Duration of ART was also considered among total patients maximum patients (27.27%) were on ART since 1 to 3 years followed by more than 60 months of ART in 23.86% of total patients. **Conclusion:** Early starting of ART leads to Increased CD4 count which lowers the incidence of tuberculosis in HIV patients.

INTRODUCTION

As per the Global TB Report 2021, the estimated incidence of all forms of TB in India for the year 2020 was 188 per 100,000 population (129-257 per 100,000 population). The total number of incident TB patients (new & relapse) notified during 2021 was 19,33,381 which was 19% higher than that of 2020 (16,28,161).^[1] An estimated one-third of the world's population is infected with Mycobacterium tuberculosis, over 10 million developed TB and 1.5 million died in 2017. People living with HIV (PLHIV) are at high risk of developing TB and account for nearly 9% of new TB cases and nearly 300,000 TB-related deaths globally.^[2] Interventions to reduce HIV associated TB include antiretroviral therapy (ART), intensified TB case finding, isoniazid preventive therapy (IPT) and infection control. The use of ART reduces the risk of developing TB by 70–90%.^[3,4] As of 2017, 1.1 million individuals were on ART in India.^[5] Although, addition of Isoniazid preventive therapy (IPT) to ART is shown to further reduce TB

incidence,^[6] only 15% of eligible patients in India were on IPT as of 2017.^[7,8] Widespread anti-retroviral therapy (ART) has significantly reduced the incidence of TB in PLHIV. However, the burden of TB remains high in this population with prevalence ranging from 3 to 72% in high burden settings.^[9] While first-line ART regimens containing a non-nucleotide reverse transcriptase inhibitor (NNRTI) have significantly reduced the burden of AIDS and non-AIDS defining events, treatment failure can occur in nearly 20% of patients, requiring a switch to a second-line protease inhibitor (PI)-based regimen.^[10] PLHIV receiving second-line regimens represent a growing and potentially high-risk population for TB. To further reduce the burden of TB, the World Health Organization (WHO) recommends isoniazid prevention therapy (IPT) for all PLHIV in high TB-burden settings.^[11] India has the third highest HIV burden and the highest TB burden globally with nearly one million new TB cases among PLHIV each year.^[12] India's National AIDS Control Organization (NACO) provides free first- and second-line ART, and has recommended IPT in all PLHIV since December 2016.^[13]

However, programmatic data on the risk of TB in PLHIV receiving first- and second-line ART in India are limited. Documenting the burden and risk factors of TB in this population, especially prior to widespread IPT implementation, will provide a baseline estimate to compare the long-term effectiveness of IPT and, inform prioritized phasing in of IPT to reduce the burden of TB among PLHIV in India. Modeling studies have suggested that expansion of ART coverage, improvement in TB diagnosis and treatment can help in drastic reduction in TB incidence and mortality.^[14] However, cohort studies across regions do not share the same enthusiasm. They have shown high initial rates of TB in the first year of starting ART followed by gradual time-dependent reduction and stabilization above the estimated background population rate.^[15] In addition, long term data on ART associated TB is limited. Median follow-up on ART in cohort studies rarely exceeds 2 years.^[16] As a result, calculation of long-term TB incidence rate is hampered due to small number of participants and events. Several factors have been associated with TB incidence among HIV positive individuals including limited functional status, very low CD4 count.^[17,18]

MATERIALS AND METHODS

We conducted a retrospective cohort study of HIV-infected adults registered at the District Hospital ART center in Koppal, India. All patients registered at the ART center received free clinical care and treatment as per national program guidelines. Prior to June 2016, ART was initiated in HIV-infected adults with a CD4+ cell count below 350 cells/mm³ regardless of symptoms, or in the event of an opportunistic infection, including TB, regardless of CD4+ cell counts. These guidelines changed in June 2016 and ART was initiated in HIV-infected adults with a CD4+ cell count below 500 cells/mm³, or in the event of an opportunistic infection regardless of CD4+ cell counts thereafter.

Study Procedures

Data for this analysis were extracted from existing ART center databases. We identified adults (≥ 18 years) who initiated first- or second-line ART from January 2021 to December 2021 at the District Hospital Koppal. ART center for inclusion in our study. We excluded participants with prevalent TB, defined as a clinical (symptom and/or chest radiograph evaluation suggestive of TB) or microbiological (Acid Fast Bacilli [AFB] on smear microscopy) diagnosis of TB or receiving TB therapy at first- or second-line ART initiation. We additionally excluded participants who were transferred to another ART center for treatment within one day of ART initiation as these participants would not be available for follow-up at

the ART clinic. Socio-demographic and clinical characteristics, and CD4+ cell counts closest to first- or second-line ART initiation were extracted for analysis. Participants with unavailable data at ART initiation were excluded.

All participants at the ART center underwent screening for TB at each clinic visit using a WHO recommended questionnaire to assess symptoms of current cough, night sweats, weight loss and fever. Participants testing positive on the symptom screening questionnaire underwent chest radiography and AFB smear microscopy on at least two clinical samples for confirmation of suspected TB. The final diagnosis of TB recorded in the ART center database was extracted for analysis. Participants lost to follow-up, defined according to NACO guidelines as missing three consecutive monthly clinic visits, were identified from the ART center database. Similarly, data on all-cause mortality was extracted from the ART center databases.

Statistical Analysis

Continuous variables were summarized using median and interquartile range (IQR), while categorical variables were summarized using frequency and percentages. Continuous variables were compared using a median test. Categorical variables were compared using Chi-square test and Fisher's exact test. TB incidence rate was defined as number of TB cases occurring per 100 person years after ART initiation. Duration of ART was calculated from date of ART initiation to development of first episode of incident TB, death of patient, lost to follow up (no clinic visits for more than 6 months) or censoring of observations on 1st March 2018. Person time accrued on ART during concomitant treatment of prevalent TB was excluded from denominator while calculating TB incidence rates. Baseline and Time dependent risk factors associated with incident TB were identified by univariate and multivariate Cox proportional hazard model. Baseline risk factors considered were age (≤ 40 years or > 40 years), gender, prevalent TB, pre-ART CD4 count ($CD4 \leq 200$ and > 200), addictions and hemoglobin (Hb < 10 g/dl or ≥ 10 g/dl). Time dependent risk factors included were current time updated CD4 count, virologic status on ART (virologically suppressed (VS) or virologic failure (VF)) and use of ART with IPT. All data was analyzed by STATA version 12.0.

RESULTS

Total 3762 HIV patients are under follow up in our ART centre among them 88(n) patients were newly detected with tuberculosis by CBNAAT and were started on Anti tubercular therapy

Table 1: Demographic details of the patients

	(n)	%
Age		
≤40 years	52	59.09%
>40 years	36	40.90%
Sex		
Male	49	55.68%
Female	39	44.31
Duration of ART		
≤ 6 month	12	13.63%
6-12 months	16	18.18%
12-36 months	24	27.27%
37-60 months	15	17.04%
>60 months	21	23.86%
Pre ART CD4 counts		
≤50	11	12.5%
51-200	46	52.27%
201-500	24	27.27%
>500	7	7.9%

Table 2: Incidence of Tuberculosis in HIV patients

Incidence of Tuberculosis in HIV patients	2.339 per 100 person years
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Among total HIV patients 88 patients were diseased with tuberculosis also in one year. among 88 patients 52 patients were of the age ≤40 years and 36 patients were of the age > 40 year. Among total patients 49 were males and 39 were females. Duration of ART was also considered among total patients maximum patients (27.27%) were on ART since 1 to 3 years followed by more than 60 months of ART in 23.86% of total patients. Among total patients maximum patients (51.27%) were having pre ART CD4 count of 51-200 cells/mm³. Incidence of Tuberculosis in HIV patients in our study is 2.339 per 100 person years.

DISCUSSION

Tuberculosis is the most common HIV-related opportunistic infection in India, and caring for patients with both diseases is a major public health challenge. India has about 1.8 million new cases of tuberculosis annually, accounting for a fifth of new cases in the world — a greater number than in any other country.^[19]

In India, tuberculosis care and HIV care are increasingly being coordinated, but the full benefits have yet to be realized. An example of successful coordination is the referral of people with suspected tuberculosis from voluntary counseling and testing centers for HIV to tuberculosis-control facilities. Between January and September 2006, a total of 15,000 people with suspected tuberculosis who were HIV-positive and 16,420 who were HIV-negative were referred to such facilities by centers in the six Indian states with the highest HIV prevalence (Andhra Pradesh, Karnataka, Maharashtra, Manipur, Nagaland, and Tamil Nadu); tuberculosis was diagnosed in 22.3% and 23.9% of patients in these groups, respectively. DOTS was begun in many of these patients. The control of both tuberculosis and HIV is likely to be most successful if programs collaborate whenever possible and are closely integrated with the rest of medical care.^[20]

Our tertiary care centre is the major tertiary care hospital in Koppal district. Caters its ART services to a total of 3762 HIV patients. In the year 2021 in our centre 88 new Tuberculosis patients were detected leading to an incidence rate of 2.339 per 100 person years which was comparable to most of the other Indian studies.^{21,22} We found 2 studies which reported the occurrence of ART associated TB from the Indian public health sector with a follow-up period of 6 months to 4 years.^[21,22] These studies observed an incidence rate of 2.4–2.83 cases per 100 person years for the entire follow-up period which is higher than that seen in our study (1.85 cases per 100 person years). Lower incidence of TB in our cohort compared to the 2 reported studies could be due to the availability of better preventive, diagnostic and treatment set-ups and strategies for controlling TB.²³ Lower incidence rate of TB could also be due to longer follow up on ART in our cohort. Drawbacks of these studies.^[21,22] Include limited follow up on ART, majority of incident TB cases occurring in first 6 months post ART, all patients with symptoms not actively investigated for TB, nonavailability of time updated CD4 count and viral load values and nonuse of culture or molecular methods for TB diagnosis. The strengths of our cohort include its large size, maintenance of electronic records of all patients, prolonged duration of follow-up (median of 5 years), annual CD4 count and pVL monitoring, intensive TB case finding by applying WHO symptom score at every clinic visit, data on use of IPT and ART and recording of treatment outcomes of patients on antitubercular therapy (ATT).^[23]

CONCLUSION

From the current study it was concluded that tuberculosis in HIV has a higher incidence. Lower the CD4 count higher was the chance of acquiring Tuberculosis. Starting ART early in treatment naïve individuals, close monitoring for incident TB in patients with low baseline and updated CD4 count,

routine virologic monitoring of all patients on ART and routine use of ART are important takeaways from our cohort study. Hence early starting of ART leads to Increased CD4 count which lowers the incidence of tuberculosis in HIV patients.

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