



## Original Research Article

## A retrospective longitudinal study on tuberculosis disease among people with HIV

Balaji G Tuppekar<sup>1,\*</sup>, Sanjay G Mutyepod<sup>2</sup>, Abhinand S Kumbar<sup>3</sup><sup>1</sup>Dept. of Pulmonary Medicine, D Y Patil Medical College, impri-Chinchwad, Maharashtra, India<sup>2</sup>Dept. of Pulmonary Medicine, Shri Vasant Rao Naik Govt. Medical College, Yavatmal, Maharashtra, India<sup>3</sup>Dept. of Repertory Medicine, A.J. Institute of Medical Sciences and Research Centre, Mangalore, Karnataka, India

## ARTICLE INFO

## Article history:

Received 25-07-2021

Accepted 20-08-2021

Available online 17-08-2022

## Keywords:

Tuberculosis (TB)

HIV

Isoniazid Prevention Therapy (IPT)

## ABSTRACT

**Background:** The use of Isoniazid Prevention Therapy (IPT) helps normalize the health issues of patients with TB. The majority of patients suffering from these diseases are from a low-income group with poor education. They do not have adequate knowledge related to prevention and approaches that reduce the occurrence of TB disease soon after ART initiation where risk is higher.

**Aim:** The study aims to determine the incidence of tuberculosis disease among patients with HIV while taking IPT and after its completion.

**Materials and Methods:** This is a retrospective, observational, longitudinal study that used existing records of patients from Department of Pulmonary Medicine, D Y Patil Medical College, Nerul, Navimumbai, Maharashtra, India. The period of the study was from January 2020 to June 2021. STATA statistical software Version 12 was used to analyse the data. The sample size was estimated based on simple proportion formula taking incident TB disease after starting IPT 1.5% based on the study in a similar setting.

**Results:** In this study, 960 patients were involved with mean age of 30 years, ranged between 25-37 years. TB was developed in 9.2% patients, out of which, 2.2% of patients were diagnosed while receiving IPT and 6.97% after IPT. Moreover, 55.2% of patients were on this treatment at the last observation. The unfavourable count of patients was 152 (15.8%). Most of the patients with unfavourable follow-up outcomes were lost to follow-up. 0.6% of patients have stopped treatment during the follow-up and 28.9% was transferred out. Finally, 4.7% of patients died and remaining were recovered.

**Conclusion:** Breakthrough TB was uncommon and shown a significant proportion of its occurrence in the first month of treatment. This could be due to difficulty in diagnosing TB disease with HIV. The proper screening of patients is essential for offering treatment and providing effective care services.

This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: [reprint@ipinnovative.com](mailto:reprint@ipinnovative.com)

## 1. Introduction

There are different types of prevention therapies used for managing and lowering the risk of TB and related diseases. The use of Isoniazid Prevention Therapy (IPT) helps normalize the health issues of patients with TB.<sup>1</sup> The majority of patients who were suffering from these diseases are from low-income groups with poor education.

They do not have adequate knowledge related to prevention and approaches that support to minimize the occurrence of TB using the ART treatment. There are several issues that are influencing the implementation of IPT. The lack of clinical treatment and issues of awareness are likely to account for a small fraction of reasons involve the lack of knowledge and proper diet as well as the side effects.<sup>2</sup> The government and medical professionals need to offer proper information about the issues and prevention methods of TB patients with HIV. The lack of support and wrong attitude

\* Corresponding author.

E-mail address: [drbalajituppekar@gmail.com](mailto:drbalajituppekar@gmail.com) (B. G. Tuppekar).

of care workers towards such patients is having a significant impact on health and recovery. They are not having serious concerns with uncertainty and ruling out the impact of TB.

A study by World Health Organization (WHO) has provided information related to the symptoms based tuberculosis screening algorithm.<sup>3</sup> The lack of knowledge treatment and planning for offering of medicines is having a negative impact on the health condition of the patients and planning of the care professionals. The current study discusses the impact of TB on the health condition of HIV patients. Practically, the incident of screening and treatment is having a significant impact on a large population as it becomes difficult for the care professionals to reach every individual. Lack of education about the symptoms and prevention methods has resulted in increasing the level of infection among people.<sup>4</sup> The compliance of HIV services in implementing LTBI screening and treatment was often unsatisfactory. TB is one of the major causes of HIV and other infection based diseases and affects the health of the individual. For analyzing the health and providing better treatment to the people with such disease, the national and local government needs to increase the education and knowledge about such issues.

## 2. Aim

The study aims to determine the incidence of tuberculosis disease among patients with HIV while taking IPT and after its completion.

## 3. Materials and Methods

This is a retrospective, observational, longitudinal study that used existing records of patients from Department of Pulmonary Medicine, D Y Patil Medical College, Nerul, Navimumbai, Maharashtra, India. The period of the study was from January 2020 to June 2021. All government hospitals have been providing chronic HIV care (including ART) and IPT for eligible clients based on the national ART and TB/HIV guidelines since 2005. ART eligibility was based on the following criteria: all WHO stage IV clients, WHO stage III clients with  $CD4 \leq 350$  and WHO stage I or II with  $CD4 \leq 200$ . In the absence of CD4 testing, all WHO stages III clients were eligible for ART. The first line ARV regimens used were according to national and international guidelines. STATA statistical software Version 12 was used to analyse the data. The sample size was estimated based on simple proportion formula taking incident TB disease after starting IPT 1.5% based on the study in a similar setting.

## 4. Results

According to Table 1, 960 patients were involved in the study and the mean age of the participants was 30 years range between 25-37 years. TB was developed in 9.2% patients, out of which, 2.2% of patients were diagnosed

while receiving IPT and 6.97% after IPT. The incidence of TB was high among these patients in the last 4 months.

As per Table 2, patients with higher baseline CD4 cell count ( $\geq 350$  cells/mm<sup>3</sup>) and those receiving ART were less likely to develop TB disease ( $P < 0.05$ ). Other variables did not have an effect on the occurrence of incident TB disease among PLHIV who took IPT ( $P > 0.05$ ).

As per Table 3, no evidence was identified for difference in risk factors and development of TB while taking IPT and after taking IPT ( $p > 0.05$ ).

Table 4 has shown the final analysis of the outcome of the patients after ART treatment 55.2% of patients were on this treatment at the last observation. Most of the patients (10.4%) with unfavourable follow-up outcomes were lost to follow-up. 0.6% of patients have stopped treatment during the follow-up and 28.9% were transferred out. However, 4.7% of patients have died and others were recovered. The unfavourable count of patients was 152 (15.8%).

As per Table 5, male was associated with increased hazard of having unfavourable final status ( $p < 0.05$ )

## 5. Discussion

According to the analysis, the breakthrough TB was uncommon among those receiving IPT in the current study. According to the outcome of the current study, 960 patients were involved in the study and the mean age of the participants was 30 years range between 25-37 years. TB was developed in 9.2% patients, out of which, 2.2% of patients were diagnosed while receiving IPT and 6.97% after IPT. The incidence of TB was high among these patients in the last 4 months.<sup>5</sup> The proper consideration of ART and CD4 cell count is helpful for planning and management of health issues of patients and better diagnose.<sup>6</sup> As per the previous study, 3142 patients were considered for diagnosing and treatment and found that 27.1% were diagnosed with TB while receiving IPT and having critical issues.<sup>7</sup>

As per the study, 55.2% of patients were on this treatment at the last observation. Most of the patients (10.4%) with unfavourable follow-up outcomes were lost to follow-up. 0.6% of patients have stopped treatment during the follow-up and 28.9% was transferred out. However, 4.7% of patients have died and others were recovered. The unfavourable count of patients was 152 (15.8%). The previous study has shown that 64% were reported with negative effects of TB and HIV and 4% have died. Moreover, 28% were lost to follow-up and 4% were transferred. In this study, most patients also received ART and thus IPT adherence may have been better.<sup>8</sup> The compliance of HIV services in implementing LTBI screening and treatment was often unsatisfactory. TB is one of the major causes of HIV and other infection based diseases and affects the health of the individual.<sup>9</sup>

**Table 1:** Baseline Demographic and Clinical Characteristics of Patients on IPT

Variable	Sub-category	Breakthrough TB (%)	TB after IPT completion (%)	Total
Age	<15	1 (1.04%)	2 (2.0%)	96
	≥15	21 (2.4%)	65 (7.4%)	864
Gender	Female	12 (2.0%)	40 (6.9%)	576
	Male	10 (2.6%)	27 (7.0%)	384
Baseline WHO Stage	I or II	8 (0.4%)	15 (3.5%)	420
	III or IV	14 (2.5%)	52 (9.6%)	540
Baseline CD4 Count	<100	7 (15.2%)	12 (47.8%)	46
	100–349	8 (1.4%)	45 (8.2%)	544
	≥350	7 (1.8%)	10 (2.7%)	370
Treatment Status	IPT only	6 (4.2%)	22 (15.7%)	140
	ART and IPT	16 (1.9%)	45 (5.4%)	820
Grand total		22 (2.2%)	67 (6.9%)	960

**Table 2:** Determinants of Occurrence of TB using isonizid preventive

Variables	Sub-category	TB	Hazard Ratio (P-value)
Age	<15	3	0.88 (0.879)
	≥ 15	86	
Gender	Female	48	1.28 (0.152)
	Male	34	
Baseline WHO stage	I or II	20	1.33 (0.365)
	III or IV	56	
Baseline CD4 count	<100	19	0.77 (0.13)
	100-349	53	
	≥ 350	17	
Treatment status	IPT only	28	.078 (<0.001)
	ART and IPT	61	

**Table 3:** Determinants of Occurrence of TB during and after IPT

Variable	Sub-category	Breakthrough TB (%)	TB after IPT completion (%)	Total	P-value
Age	<15	1 (1.04%)	2 (2.0%)	96	0.085
	≥15	21 (2.4%)	65 (7.4%)	864	
Gender	Female	12 (2.0%)	40 (6.9%)	576	0.356
	Male	10 (2.6%)	27 (7.0%)	384	
Baseline WHO Stage	I or II	8 (0.4%)	15 (3.5%)	420	0.154
	III or IV	14 (2.5%)	52 (9.6%)	540	
Baseline CD4 Count	<100	7 (15.2%)	12 (47.8%)	46	0.232
	100–349	8 (1.4%)	45 (8.2%)	544	
	≥350	7 (1.8%)	10 (2.7%)	370	
Treatment Status	IPT only	6 (4.2%)	22 (15.7%)	140	0.207
	ART and IPT	16 (1.9%)	45 (5.4%)	820	
Grand total		22 (2.2%)	67 (6.9%)	960	

**Table 4:** Final status

Last status	Frequency	Percentage	Cumulative percentage
Died	46	4.7	2
Lost to follow-up	100	10.4	10
Stopped treatment	6	0.6	10
Transferred out	278	28.9	18
Active	530	55.2	100

**Table 5:** Unfavourable final status

Variables	Sub-category	Unfavourable outcome	Hazard Ratio (P-value)
Age	<15	12	1
	≥ 15	140	1.12 (0.89)
Gender	Female	80	1
	Male	72	1.55 (<0.001)
Baseline WHO stage	I or II	67	1
	III or IV	85	1.21 (0.089)
Baseline CD4 count	<100	52	1
	100-349	90	0.81 (0.066)
	≥ 350	10	0.59 (0.086)
Treatment status	TB after IPT completion	2	1
	No TB	146	0.51 (0.06)
	Breakthrough TB	4	2.25 (0.11)

Our results showed that HIV patients never tested for LTBI and those who tested positive at the first instance were at higher risk of TB disease development.<sup>10</sup>

## 6. Conclusion

From the study, it has been carried out that breakthrough TB was uncommon and showing the significant proportion of it occurred in the first month of treatment and could be due to difficulty in diagnosing TB disease with HIV. The proper screening of patients is essential for offering treatment and providing effective care services. Moreover, the lack of education and awareness about the issues that could lead to serious illness are the major issues. The proper investigation and follow-up of such patients are important for preventing infection and maintaining good standards of health.

## 7. Source of Funding

No financial support was received for the work within this manuscript.

## 8. Conflict of Interest

The authors declare they have no conflict of interest.

## References

- Yirdaw KD, Teklu AM, Mamuye AT, Zewdu S. Breakthrough tuberculosis disease among people with HIV-Should we be worried? A retrospective longitudinal study. *PLoS One*. 2019;14(2):e211688. doi:10.1371/journal.pone.0211688.
- Luboga SA, Stover B, Lim TW, Makumbi F, Kiwanuka N, Lubega F, et al. Did PEPFAR investments result in health system strengthening? A retrospective longitudinal study measuring non-HIV health service utilization at the district level. *Health Policy Plan*. 2016;31(7):897–909. doi:10.1093/heapol/czw009.
- Otero L, Shah L, Verdonck K, Battaglioli T, Brewer T, Gotuzzo E. A prospective longitudinal study of tuberculosis among household contacts of smear-positive tuberculosis cases in. *BMC Infect Dis*. 2016;16(1):1–8.

- Ranzani OT, Rodrigues LC, Bombarda S, Minto CM, Waldman EA, Carvalho CR, et al. Long-term survival and cause-specific mortality of patients newly diagnosed with tuberculosis in São Paulo state, Brazil, 2010-15: a population-based, longitudinal study. *Lancet Infect Dis*. 2020;20(1):123–32.
- Van Der Heijden YF, Karim F, Chinappa T, Mufamadi G, Zako L, Shepherd BE, et al. Older age at first tuberculosis diagnosis is associated with tuberculosis recurrence in HIV-negative persons. *Int J Tuberc Lung Dis*. 2018;22(8):871–7.
- Hassan AS, Bibby DF, Mwaringa SM, Agutu CA, Ndirangu KK, Sanders EJ, et al. Presence, persistence and effects of pre-treatment HIV-1 drug resistance variants detected using next generation sequencing: A Retrospective longitudinal study from rural coastal Kenya. *PLoS One*. 2019;14(2):e210559. doi:10.1371/journal.pone.0210559.
- Gomes N, Bastos M, Marins RM, Barbosa AA, Soares LCP, De Abreu A, et al. Differences between risk factors associated with tuberculosis treatment abandonment and mortality. *Pulm Med*. 2015;p. 546106. doi:10.1155/2015/546106.
- Roth PJ, Grim SA, Gallitano S, Adams W, Clark NM, Layden JE, et al. Serial testing for latent tuberculosis infection in transplant candidates: a retrospective review. *Transplant Infect Dis*. 2016;18(1):14–21.
- Rich AJ, Williams J, Malik M, Wirtz A, Reisner S, Dubois LZ, et al. Biopsychosocial mechanisms linking gender minority stress to HIV comorbidities among Black and Latina Transgender Women (LITE Plus): protocol for a mixed methods Longitudinal Study. *JMIR Res Protoc*. 2020;9(4):e17076. doi:10.2196/17076.
- García JJ, Mambuque E, Nguenha D, Vilanculo F, Sacooc C, Sequera VG, et al. Mortality and risk of tuberculosis among people living with HIV in whom TB was initially ruled out. *Scientific Rep*. 2020;10(1):1–11.

## Author biography

**Balaji G Tuppekar**, Assistant Professor

**Sanjay G Mutyepod**, Assistant Professor

**Abhinand S Kumbar**, Assistant Professor

**Cite this article:** Tuppekar BG, Mutyepod SG, Kumbar AS. A retrospective longitudinal study on tuberculosis disease among people with HIV. *Panacea J Med Sci* 2022;12(2):237-240.