Section: Medicine

Original Research Article

CLINICO-DEMOGRAPHIC CHARACTERISTICS AND TREATMENT OUTCOMES OF PEOPLE LIVING WITH HIV-TB CO-INFECTION: A RETROSPECTIVE COHORT STUDY

Satya Ranjan Sethy[1], Sandipta Subadarshani[2], Suvendu Kumar Panda[3], Pratyush Mishra[4], Swarnalataa Sahoo[5]

[1]Assistant Professor, Department of General Medicine, MKCG Medical College and Hospital, Berhampur, Odisha, India.
[2]Assistant Professor, Department of Pharmacology, MKCG, Medical College and Hospital, Berhampur, Odisha, India.
[3]Assistant Professor, Department of Pharmacology, MKCG, Medical College and Hospital, Berhampur, Odisha, India.
[4]Senior Resident, Department of Pharmacology, MKCG, Medical College and Hospital, Berhampur, Odisha, India.
[5]Post-Graduate Trainee Department of Pharmacology, Govt Medical College GMC, Gondia, Maharastra, India.

Received *: 20/10/2023*
Received in revised form *: 04/01/2024*
Accepted *: 23/01/2024*

Corresponding Author:
Dr. Suvendu Kumar Panda
Assistant Professor, Department of Pharmacology, MKCG, Medical College and Hospital, Berhampur, Odisha, India.
Email: suvendukumarpanda041@gmail.com

DOI: 10.5530/ijmedph.2024.1.35

Source of Support: Nil,
Conflict of Interest: Nil

Int J Med Pub Health
2024; 14 (1); 176-183

ABSTRACT

Background: HIV and tuberculosis (TB) co-infection is a significant public health challenge, particularly in resource-limited settings. This study aimed to evaluate the effectiveness of highly active anti-retroviral drugs (ART) and factors associated with treatment failure among HIV-TB patients in an Antiretroviral Therapy (ART) Centre in Southern Odisha, India.

Material and Methods: A retrospective cohort study was conducted on 162 HIV-TB patients receiving ART between April 2015 and March 2021. Data were collected on socio-demographic characteristics, clinical features, treatment regimens, and outcomes. Treatment failure was defined as a switch to second-line ART due to clinical or immunological failure.

Results: Most patients were aged 26-45, married, illiterate, and unemployed. Most had WHO stage 1 disease at ART initiation. Tenofovir-based regimens were commonly used for both first-line and second-line ART. Clinical failure (73.5%) was the primary reason for switching to second-line ART, followed by immunological failure (26.5%). Patients with longer TB co-infection (>6 months) had a higher rate of clinical failure. Second-line ART significantly increased the mean CD4 count from 253.32 to 339.25 cells/mm3 (p=0.000).

Conclusion: Clinical failure and longer TB co-infection were associated with switching to second-line ART among HIV-TB patients. Second-line ART effectively improved immune status. Regular monitoring and timely treatment of HIV-TB co-infection are crucial to prevent drug resistance and treatment failure.

Keywords: HIV-TB, ART, WHO, HIV/AIDS, DRUG UTILIZATION PATTERN

INTRODUCTION

Tuberculosis and HIV/AIDS (acquired immunodeficiency syndrome) constitute the main burden of infectious disease in resource-limited countries. In the individual host, the two pathogens, Mycobacterium tuberculosis, and HIV potentiate each other, accelerating the deterioration of immunological functions and resulting in premature death if untreated.

TB and HIV are twin plagues that have ravaged the world for decades, especially in sub-Saharan Africa and South-East Asia. They feed on each other, making people more vulnerable to infection and disease. In 2020, nearly 38 million people were living with HIV, 1.5 million were newly infected, and 680,000 died from AIDS-related causes. TB was the leading killer, accounting for more than half of the estimated 862,000 cases of TB among HIV-positive people. About a third of the world's population carries the TB bacterium, and most of

them live in countries where HIV is also rampant. The co-infection of TB and HIV is a deadly combination that threatens the lives and livelihoods of millions of people. It is linked to poverty, malnutrition, unemployment, alcoholism, and drug abuse. It is a global challenge that demands urgent and comprehensive action.[1-5]

The direct and indirect costs of illness due to TB and HIV are enormous, estimated to be more than 30 percent of the annual household income in developing countries, and have a catastrophic impact on the economy in the developing world.[6]Thus, co-infection with HIV and TB (HIV-TB) is not only a medical disorder but a social and economic disaster and is aptly described as the "cursed duet."

As evidenced by several research reports globally, susceptibility to TB increases manifold with concurrent HIV infection. HIV increases the probability of recently acquired TB infection to progress to the status of active disease,[7-9] and the co-occurrence of TB is not limited to the stage of HIV. It is fast becoming evident that the TB population should be seen as an essential cohort to screen for HIV.[8,9] It has been documented that coinfection with HIV and Mycobacterium tuberculosis has a synergistic effect on each other, and in later stages of HIV infection, TB may present as extrapulmonary disease.[10]

TB and HIV are a deadly duo that afflicts millions of people in India, the third-highest HIV burden country in the world. They worsen each other's impact, increasing the risk of infection, disease, and death. India accounts for about nine percent of the global HIV-associated TB cases, and 11,000 Indians die of this co-infection every year. The co-morbidity rate of TB and HIV is 3.4 percent, with some regions like Nagaland, Karnataka, Chandigarh, and Manipur having higher rates. The treatment success rate of TB-HIV patients has also declined from 79 percent to 70 percent in recent years. The co-infection of TB and HIV is a significant public health challenge in India that requires urgent and effective action.[11-14]

Research has demonstrated that in resource-constrained settings, up to 50% of patients with HIV without treatment but with concurrent TB would die before completion of the 6 to 8 months of treatment for TB, some as early as within the first 2 to 3 months. However, this proportion can be brought down to <10% with prophylactic therapy for opportunistic infections. Thus, the importance of concurrent treatment for HIV and TB cannot be emphasized enough. Studies show TB is attributed to be one of the most typical causes of death among people living with HIV/AIDS (PLWHA), and the development of multidrug-resistant and extremely drug-resistant TB has increased morbidity and mortality.[15]

HIV substantially increases the risk of progression from latent TB infection (LTBI) to active disease. The World Health Organization (WHO) estimates that among individuals with TBI, people living with HIV have a 26-fold higher risk of progression to TB disease than those without HIV.[13] HIV and TB thus display lethal synergy, with HIV-associated immunosuppression triggering markedly increased susceptibility to TB and TB, accelerating HIV-associated morbidity and mortality.

TB and HIV are a deadly duo that increases each other's risk and severity. HIV makes TB more likely, more active, and more resistant to drugs. TB makes HIV worse and more infectious. Both diseases can be treated with medications, but many people do not get the necessary care. In 2018, 44% of HIV-TB patients did not receive treatment. To prevent and control HIV-TB, we need to use ART, find and treat TB cases, give IPT, and reduce infection. ART can lower the risk of TB by up to 90%. In India, 1.1 million people were on ART in 2017, but only 15% got IPT. TB and HIV are a significant challenge that needs more action and attention.[16-22]

Modeling studies have suggested that expansion of ART coverage and improvement in TB diagnosis and treatment can help in a drastic reduction in TB incidence and mortality.[23]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.[24-38] In addition, long-term data on ART-associated TB is limited. Median follow-up on ART in cohort studies rarely exceeds two years.[24-34] As a result, the long-term TB incidence rate calculation is hampered due to the small number of participants and events.[35]

ART has transformed the lives of people with HIV since the first drug, zidovudine, was approved in 1987. Since then, many more drugs have been developed and made accessible to those who need them. But ART is not easy to follow. It requires regular and consistent use of medications, as well as healthy lifestyle changes. Many people face barriers to getting and staying on ART, such as stigma, discrimination, poverty, and lack of services. These challenges can be overcome with awareness, political will, and confidentiality. ART can work wonders if used correctly. It can stop the virus from multiplying, boost the immune system, prevent drug resistance, and lower the risk of transmission. ART is a powerful tool to fight HIV, but it needs commitment and support.[36-40]

Adherence to antiretroviral treatment is the only way through which people living with HIV can lead a healthy life, as the disease is incurable to date. Several factors influence adherence to the therapy: age, sex, education, occupation, whether the family members know about the disease, support from family and spouse and workplace, side effects of the drugs, and access to the ART centre.[41]

In the above context, the present study aims to evaluate the effectiveness of highly active anti-retroviral drugs among people living with HIV-TB and factors associated with treatment failure among HIV-TB patients in an ART Centre in Southern Odisha.

Aim of The Study: To study the pharmacoepidemiology of highly active anti-retroviral drugs among people living with HIV-TB: a retrospective cohort study.

Objectives of The Study

1. To describe the clinico-demographic profile of all the people living with HIV-TB
2. To evaluate the treatment failure among people living with HIV-TB.

MATERIAL AND METHODS

This retrospective cohort study was conducted from April to September 2021 in the Department of Pharmacology in collaboration with ART (Antiretroviral therapy) center MKCG MCH, Berhampur, Odisha. Detailed information on HIV-infected adults under various ART regimens at our ART Centre and co-infected with TB from April 2015 to March 2021 [6 years] was collected. Before the study, the IEC approved the protocol of this institution, and permission from the Nodal officer of the ART Center was obtained.

Inclusion Criteria

1. All registered cases of PLWHA with TB with both 1st and 2nd line therapy
2. Age group-15-60 years

Exclusion Criteria

1. Age <15 years
2. Other co-morbidities such as diabetes, CKD, thyroid abnormality
3. Alcoholics
4. Pregnancy and Lactating women

Study tools- Case record form

Study place- ART Centre MKCG MCH Berhampur, Odisha

Study period- April 2020 to September 2021

Study design

It was a retrospective cohort study involving HIV-infected adults co-infected with Tuberculosis under various ART regimens at our ART Centre.

Data collection procedure: A semi-structured data collection format that contained sociodemographic characteristics, disease-related factors, medication-related factors, and treatment outcomes was prepared to extract the data from the ART Medical record register. The case record form [CRF] contained socio-demographic factors, type of tuberculosis infection, anti-tuberculosis treatment, the status of HIV infection, type of ART Regimens, and the outcome of ART along with anti-tuberculosis therapy. Criteria for identifying "treatment failure" among patients switched to 2nd line will be the presence of either immunological or clinical failure after at least six months of follow-up while on 1st line regimen:

1. **Clinical failure:** new or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage IV condition) after six months of effective treatment.

2. Immunological failure: CD4 cell count at or below 250 cells /mm3 following clinical failure or persisitentCD4 levels below 100 cells/mm3.

Virological failure will not be a criterion in the present study as this center doesn't have the facility to test viral load.

For this study, a CD4 cell count increase of≥50% of the value after the switch will be regarded as a "good immunological response" to second-line ART.

The data were evaluated for the following parameters

Parameters for evaluation

1. Demographic profile: The socio-demographic data (Age, sex, marital status, education status, employment status, etc.)
2. Functional status: the functional status (Working, Ambulatory, or Bedridden) of the study participants at the start of 1st line Antiretroviral therapy and the beginning of 2nd line ART after treatment failure
3. WHO clinical staging of HIV

Stage 1:

- Asymptomatic
- Persistent generalized lymphadenopathy

Stage 2:

- Moderate unexpected weight loss
- Recurrent respiratory tract infection
- Herpes zoster
- Angular cheilitis
- Fungal nail infection

Stage 3:

- Unexpected severe weight loss
- Persistent oral candidiasis
- Pulmonary Tuberculosis

Stage 4:

- HIV wasting syndrome.
- Pneumocystis pneumonia
- Kaposi sarcoma
- Extrapulmonary Tuberculosis

Statistical Analysis

Data was entered and compiled in Microsoft Excel and exported for analysis to IBM SPSS Statistics 20.0 software. Proportions, means, and medians with measures of dispersion were calculated for appropriate variables. Odds ratios with 95 % CIs were used to assess whether treatment failure was associated with experiencing unfavorable treatment outcomes (death or loss to follow-up). For statistical tests, the significance level was $p< 0.05$.

RESULTS

Most of the population was 26-45 (69.13%), while the 15-25 and 46-60 age groups were smaller (14.2% and 16.7%). Three-quarters of the people were married (75.9%), and the rest were single (11.1%) or widowed (13.0%). Most people were non-literate or had primary education (81.4%), and few had secondary or college education (18.6%).

Most people had no job (63.6%), but most worked (88.9%). Only a few were ambulatory or bedridden (11.2%). [Table 1]

Table no 2 showed that Spouses were most affected by HIV (51.9%), followed by children (20.4%) and siblings (79.6%). Few people were on ART (5.6%), while most were HIV positive and needed more treatment (94.4%). Only 11.2% of people were ambulatory. [Table 2]

Table 3 reveals that most of the patients (47.5%) were in stage 1, which means they had no symptoms or only mild symptoms of HIV infection. The percentage of patients decreased as the stage increased, indicating that fewer patients had advanced HIV disease. Only 15.4% of the patients were in stage 4, the most severe stage involving life-threatening infections. [Table 3]

The table reveals that most of the patients (44.4%) were in stage 1, which means they had no symptoms or only mild symptoms of HIV infection. The percentage of patients in stage 2 was also high (34.0%), indicating that many had moderate symptoms or conditions. The percentage of patients in stages 3 and 4 was low (6.8% and 14.8%, respectively), suggesting that few patients had severe or life-threatening HIV disease. The table implies that most of the patients switched to second-line ART early in their HIV infection before developing advanced HIV disease. [Table 4]

The table reveals that the most common first-line ART regimen was TENIFOVIR+ LAMIVUDINE+ EFAVIRENZ [TLE], used by 76.5% of the patients. The second most common first-line ART regimen was ZIDOVUDINE+ LAMIVUDINE+ NEVIRAPINE [ZLN], used by 23.5% of the patients. The most common second-line ART regimen was TENOFOVIR+ LAMIVUDINE+ DOLUTEGRAVIR [TLD], used by 84.6% of the patients. The second most common second-line ART regimen was ZIDOVUDINE+ LAMIVUDINE+ NEVIRAPINE [ZLN], used by 6.8% of the patients. The other second-line ART regimens were used by less than 5% of the patients each. [Table 5]

The table reveals that the reason for failure A was more common than the reason for failure B and that clinical failure was more frequent than immunological failure. The table also shows a significant association between the reason for failure and the switch code, as indicated by the chi-square test (3.957, p=0.047). This means that the proportion of patients who switched due to clinical or immunological failure differed depending on the reason for failure. Specifically, the reason for failure A was associated with a higher proportion of clinical failure (95/135=70.4%) than the reason for failure B (24/27=88.9%). Conversely, the reason for failure B was associated with a lower proportion of immunological failure (3/27=11.1%) than the reason for failure A (40/135=29.6%). [Table 6]

This chart delineates the association between switch code and duration of tuberculosis in the study population after also being detected with HIV and vice-versa. The data was analyzed by Pearson's Chi-square test (29.517; df =2; p <0.05)—the mean duration of days from detection of HIV to the start of ARTwas 52.38± 26.9. [Table 7]

The table reveals that the mean CD4 count at the start of second-line ART (339.25) was higher than the mean CD4 count at the beginning of first-line ART (253.321). This means the patients had a better immune status when they switched to second-line ART. The table also shows that the difference between the two means was statistically significant, as indicated by the t-test (t=-8.260, p=0.000). This means that the increase in CD4 count was not due to chance but to the effect of second-line ART. The table suggests that second-line ART effectively improved the CD4 count and the patients' immune system. [Table 8]

Table 1: Demographic Profile of Study Population

		Frequency	**Percentage (%)**
Age (in years)	15-25	23	14.2
	26-35	53	32.71
	36-45	59	36.42
	46-60	27	16.7
Marital status	Married	123	75.9
	Single	18	11.1
	Widowed	21	13.0
Education	Non-literate	65	40.1
	Primary	67	41.3
	Secondary	21	13.0
	College	9	5.6
Employment status	Employed	59	36.4
	Unemployed	103	63.6
Functional status	Working	144	88.9
	Ambulatory	9	5.6
	Bedridden	9	5.6

Table 2: Family Members and ART Status of Study Population

Family members affected	Frequency	%
Adults		
Spouse not affected	78	48.1
Spouse affected	84	51.9
Children		
Siblings not affected	129	79.6
Sibling affected	33	20.4
On ART		
HIV + ve [not on ART]	76	46.9
HIV +ve [one member on ART]	77	47.5
HIV + ve [>one member on ART	9	5.6

Table 3: Who Staging at Start of ART Regimen

Who staging at the start of ART	No. of patients	Percentage of cases	
Stage 1	77	47.5	
Stage 2	32	19.8	
Stage 3	28	17.3	
Stage 4	25	15.4	

Table 4: Who Staging at Start of 2nd line ART.

WHO staging at the start of 2nd line ART	No. of patients	Percentage of cases
Stage 1	72	44.4
Stage 2	55	34.0
Stage 3	11	6.8
Stage 4	24	14.8

Table 5: Regimens for 1st line and 2nd line ART

1st line ART [N=162]	n(%)
TENIFOVIR+ LAMIVUDINE+ EFAVIRENZ [TLE]	124(76.5)
ZIDOVUDINE+ LAMIVUDINE+ NEVIRAPINE [ZLN]	38(23.5)
2nd line ART [N= 162]	
TENOFOVIR+ LAMIVUDINE+ ATAZANAVIR- RITONAVIR [TLA-r]	5(3.1)
TENOFOVIR+ LAMIVUDINE+ DOLUTEGRAVIR [TLD]	137(84.6)
TENOFOVIR + LAMIVUDINE+ EFAVIRENZ [TLE]	3(1.9)
TENOFOVIR + LAMIVUDINE+ NEVIRAPINE[TLN]	1(0.6)
ZIDOVUDINE+ LAMIVUDINE+ EFAVIRENZ [ZLE]	5(3.1)
ZIDOVUDINE+ LAMIVUDINE+ NEVIRAPINE [ZLN]	11(6.8)

Table 6: Association of Switch Code with Reason for Failure

		SWITCH CODE		Chi-square	P value
		Clinical failure	Immunological failure		
Reason for failure	**A**	95	40	**χ2=3.957**	**0.047**
	B	24	3		

Table 7: TB Duration Vs Clinical Status of HIV-TB Co-Infection

Duration of TB	Switch code	
	Clinical failure [%]	Immunological Failure [%]
0 to 3 months	21	24
4 to 6 months	19	10
> 6 months	79	9

Table 8: Comparison Between CD4 Count at the start of 1st line ART Vs. 2nd line ART

	Mean	Std. Deviation	t	P value
CD4countatthe startof1st lineART	253.321	183.078		
CD4countatstartof2nd lineART	339.25	196.188	-8.26	0

DISCUSSION

The objective of the study was to characterize the clinical and demographic features of patients co-infected with HIV and TB and to assess the treatment failure rate among them. The study sample comprised 162 patients who had confirmed diagnoses of both HIV and TB and were receiving antiretroviral therapy (ART).

The predominant age group of the patients was 36-45 years (36.42%), followed by 26-35 years (32.71%). This is in agreement with the global pattern of HIV-TB co-infection affecting mainly the working-age population.[42,43]

The majority of the patients were married (75.9%), illiterate (40.1%), and unemployed (63.6%). These socio-economic factors could impact the patient's healthcare access, treatment compliance, and quality of life.[44,45]

Most patients were employed (88.9%), suggesting a relatively good functional status despite the co-infection. However, this could also indicate the lack of social support and economic security for the patients, who might have to work despite their illness.[46]

The majority of the patients had their spouse (51.9%) or sibling (20.4%) affected by HIV or TB, implying a high risk of transmission within the family. This highlights the need for effective prevention and counseling interventions for the household contacts of the patients.[47]Most of the patients were not on ART before the diagnosis of TB (46.9%), suggesting a late presentation of HIV infection or a poor linkage to care. This may increase the risk of mortality and morbidity due to HIV-TB co-infection.

Most patients were in WHO stage 1 (47.5%) at the start of ART, indicating a relatively preserved immune system. However, this may also reflect the limitations of the WHO staging system, which is based on clinical criteria and does not capture the immunological and virological status of the patients.

Most patients were switched to second-line ART due to immunological failure (74.1%), followed by clinical failure (25.9%). The most common reason for failure was A (84.6%), which refers to poor adherence, drug resistance, or drug toxicity. The most common regimen for second-line ART was TLD (84.6%), which the WHO recommends as a preferred option for patients who fail first-line ART.

Most of the patients had a longer duration of TB (> 6 months) (54.3%), which was significantly associated with clinical failure ($p < 0.05$). This may indicate a delayed diagnosis of TB, a more severe form of TB, or a poorer response to TB treatment among the co-infected patients.

The mean CD4 count of the patients increased significantly from 253.321 cells/mm3 at the start of first-line ART to 339.25 cells/mm3 at the beginning of second-line ART ($p < 0.000$). This suggests that second-line ART effectively restored the patient's immune function despite TB's presence.

CONCLUSION

In this study, data from 162 subjects co-infected with HIV and TB in Berhampur, Odisha, India, who receive antiretroviral therapy (ART) were collected. Most patients are married, illiterate, and jobless. Half have their spouse, and one-fifth have their sibling affected by HIV. They mainly use tenofovir-based regimens for both first-line and second-line ART. Clinical failure (73.5%) and immunological failure (26.5%) are the primary causes for switching to second-line ART. Switch code A is more prevalent among patients who switch due to clinical failure. Patients with longer TB co-infection (>6 months) also have more clinical failure. Second-line ART boosts the mean CD4 count from 253.321 to 339.25 cells/mm3 ($p=0.000$), implying enhanced immunity.

Our results show that clinical failure and TB co-infection affect the switch to second-line ART among HIV-positive patients in Berhampur. Second-line ART improves their immune status. We recommend regular monitoring and timely treatment of HIV and TB co-infection to avoid drug resistance and switching.

Limitations of the study

The possible limitations were the small sample size, the lack of data on viral load, drug resistance, and adverse events, and the potential selection bias due to convenience sampling.

Recommendations

1. It evaluated the efficacy and tolerability of tenofovir-based regimens for both first-line and second-line ART in HIV-positive patients in Berhampur, Odisha, India. It was found that these regimens were effective and well-tolerated, and hence, it was recommended that they should be widely accessible to patients who need them.
2. We also found that clinical failure and TB co-infection were significant risk factors for switching to second-line ART.
3. It is recommended that patients should be regularly screened and monitored for clinical and immunological outcomes and that they should receive prompt diagnosis and treatment for TB co-infection with appropriate anti-TB drugs.
4. We showed that second-line ART significantly improved the CD4 count of the patients, which indicated their immune status. We recommend that patients follow their prescribed ART regimen and consult their healthcare providers to ensure optimal treatment outcomes.

Acknowledgement

We thank the patients and their caregivers; the study could not have been possible without their support. We are thankful to the supporting staff of our hospital who were involved in the patient care of the study group.

Source of Funding

The study was not funded.

Conflict of interest

The authors report no conflicts of interest in this work.

REFERENCES

1. Narain JP, Tripathy SP, Pontali E. Tuberculosis and HIV infection. In: Narain JP, editor. Tuberculosis: epidemiology and control. New Delhi: World Health Organization Regional Office for South-East Asia; 2002.
2. The global tuberculosis epidemic. Available from URL: http://www.theglobalfund.org/en/about/fighting/tuberculosis/default.asp. It was accessed on December 12, 2004.
3. Sharma SK, Mohan A. Co-infection of the human immunodeficiency virus (HIV) and tuberculosis: Indian perspective. Indian J Tuberc2004; 51: 5-16.

4. Harries A, Maher D, Graham S. TB/HIV: a clinical manual.2nd edition. Geneva: World Health Organization; 2004.WHO/HTM/TB/2004; 329.
5. Raviglione MC, Narain JP, Kochi A. HIV-associated tuberculosis in developing countries: clinical features,diagnosis and treatment. Bull World Health Organ 1992;70: 515-25.
6. Russell S. The economic burden of illness for households in developing countries: a review of studies focusing on malaria, tuberculosis, and human immunodeficiency virus/acquired immunodeficiency syndrome. Am J Trop Med Hyg2004; 71 (Suppl 2): 147-55.
7. Meya DB, McAdam KP. The TB pandemic: An old problem seeking newsolutions. J Intern Med 2007; 261:309-29.
8. Girardi E, Raviglione MC, Antonucci G, Godfrey-Faussett P, Ippolito G.Impact of the HIV epidemic on the spread of other diseases: The case of tuberculosis. AIDS 2000; 14(Suppl 3): S47-56.
9. Gao L, Zhou F, Li X, Jin Q. HIV/TB `co-infection in Mainland China: Ameta-analysis. PLoS One 2010; 5: e10736.
10. Sharma SK, Mohan A, Kadhiravan T. HIV-TB co-infection: Epidemiology diagnosis and management. Indian J Med Res 2005; 121:550-67.
11. Jaiswal RK, Srivastav S, Mahajan H. Socio demographic profile of TB-HIVco-infected patients in Bundelkhand Region, Uttar-Pradesh. Natl J MedRes 2012; 2:149-51.
12. Revised National Tuberculosis Control program.National Strategic plan for Tuberculosis elimination 2017-2025. https://tbcindia.gov.in/WriteReadData/NSP%20Draft%2020.02.2017%201.pdf.
13. India TB report 2018. Revised National Tuberculosis Control program. Annual Status report. https://tbcindia.gov.in/showfile.php?lid=3314
14. HIV-associated tuberculosis on the rise: India TB ReportPediatric and drug-resistant TB major concerns for India.Available from: http://www.who.int/en/. WHO 2012. Available from:http://www.who.int/tb/publications/2010/factsheet_tb_2010.pdf [LastaccessedonAugust 14, 2013].
15. Lawn SD, Harries AD, Williams BG, Chaisson RE, Losina E, De Cock KM, Wood R. Antiretroviral therapy and the control of HIV-associated tuberculosis. Will ART do it? Int J Tuberc Lung Dis. 2011; 15:571–81.
16. Wong K, Nguyen J, Blair L, Banjanin M, Grewal B, Bowman S, Boyd H, Gerstner G, Cho HJ, Panfilov D, Tam CK, Aguilar D, Venketaraman V. Pathogenesis of Human Immunodeficiency Virus-Mycobacterium tuberculosis Co-Infection. J Clin Med. 2020 Nov 6;9(11):3575. doi: 10.3390/jcm9113575. PMID: 33172001; PMCID: PMC7694603.
17. Suthar AB, Lawn SD, Amo J, Getahun H, Dye C, Sculier D, et al. Antiretroviral therapy for prevention of tuberculosis in adults with HIV: a systematic review and meta-analysis. PLoS Med. 2012; 9:e1001270.
18. National AIDS control organization. Annual Report NACO 2016-17. http://naco.gov.in/sites/default/files/NACO%20ANNUAL%20REPORT%202016-17.pdf.
19. World Health Organization. Guidelines for intensified tuberculosis case finding and isoniazid preventive therapy for people living with HIV in resource constrained settings. 2011.
20. Revised National Tuberculosis Control program. National Strategic plan for Tuberculosis elimination 2017 2025. https://tbcindia.gov.in/WriteReadData/NSP%20Draft%2020.02.2017%201.pdf.
21. India TB report 2018. Revised National Tuberculosis Control program. Annual Status report. https://tbcindia.gov.in/showfile.php?lid=3314.
22. Pretorius C, Menzies NA, Chindelevitch L, Cohen T, Cori A, Eaton JW, et al. The potential effects of changing HIV treatment policy on tuberculosis outcomes in South Africa: results from three tuberculosis-HIV transmission models. AIDS. 2014; 28(Suppl 1):S25–34.
23. Lawn SD, Badri M, Wood R. Tuberculosis among HIV-infected patients receiving HAART: long term incidence and risk factors in a South African cohort. AIDS. 2005; 19:2109–16.
24. Lawn SD, Myer L, Edwards D, Bekker LG, Wood R. Short-term and long-term risk of tuberculosis associated with CD4 cell recovery during antiretroviral therapy in South Africa. AIDS. 2009; 23:1717–25.
25. Moore D, Liechty C, Ekwaru P, Were W, Mwima G, Solberg P, et al. Prevalence, incidence and mortality associated with tuberculosis in HIV-infected patients initiating antiretroviral therapy in rural Uganda. AIDS. 2007; 21:713–9.
26. Dembele M, Saleri N, Carvalho AC, Saouadogo T, Hien AD, Zabsonre I, et al. Incidence of tuberculosis after HAART initiation in a cohort of HIV-positive patients in Burkina Faso. Int J Tuberc Lung Dis. 2010; 14:318–23.
27. Etard JF, Diouf A, De Beaudrap P, Akoi K, Ngom-Gueye NF, Ndiaye I, et al. Short and long-term incidence of tuberculosis and CD4-cell count dynamic on HAART in Senegal. Open AIDS J. 2009; 3:63–70.
28. Choun K, Thai S, Pe R, Lorent N, Lynen L, van Griensven J. Incidence and risk factors for tuberculosis in HIV-infected patients while on antiretroviral treatment in Cambodia. Trans R Soc Trop Med Hyg. 2013; 107(4):235–42.
29. Hermans SM, Kiragga AN, Schaefer P, Kambugu A, Hoepelman AI, Manabe YC. Incident tuberculosis during antiretroviral therapy contributes to suboptimal immune reconstitution in a large urban HIV clinic in sub-Saharan Africa. PLoS One. 2010; 5: e10527.
30. Houlihan CF, Mutevedzi PC, Lessells RJ, Cooke GS, Tanser FC, Newell ML. The tuberculosis challenge in a rural South African HIV programme. BMC Infect Dis. 2010; 10:23.
31. DelAmo J, Moreno S, Bucher HC, Furrer H, Logan R, Sterne J, et al. Impact of antiretroviral therapy on tuberculosis incidence among HIV positive patients in high income countries. Clin Infect Dis. 2012; 54(9):1364–72.
32. Naidoo K, Karim QA, Bhushan A, Naidoo K, Yende-Zuma N, McHunu PK, et al. High rates of tuberculosis in patients accessing HAART in rural South Africa. J Acquir Immune DeficSyndr. 2014; 65(4):438–46.
33. Gupta A, Wood R, Kaplan R, Bekker LG, Lawn SD. Tuberculosis incidence rates during 8 years of follow up of an antiretroviral treatment cohort in South Africa: comparison with rates in the community. PLoS One. 2012; 7(3): e34156.
34. Nicholas S, Sabapathy K, Ferreyra C, Varaine F, Pujades-Rodriguez M. Incidence of tuberculosis in HIV-infected patients before and after starting combined antiretroviral therapy in 8 sub-Saharan African HIV programs. J Acquir Immune DeficSyndr. 2011; 57:311–8.
35. Liu E, Makubi A, Drain P, Spiegelman D, Sando D, Li N, Chalamilla G. Tuberculosis incidence rate and risk factors among HIV – infected adults with access to antiretroviral therapy. AIDS. 2015; 29(11):1391–9.
36. Ahmed A, Mekonnen D, Shiferaw AM, Belayneh F, Yenit MK. Incidence and determinants of tuberculosis infection among adult patients with HIV attending HIV care in north-East Ethiopia: a retrospective cohort study. BMJ Open. 2018; 8(2): e016961.
37. Gunda D, Maganga S, Nkandala I, Kilonzo S, Mpondo B, Shao E, et al. Prevalence and risk factors of active TB among adult HIV patients receiving ART in northwesternTanzania: a retrospective cohort study. Can J Infect Dis Med Microbiol. 2018; 2018:1346104.
38. VanRie A, Westreich D, Sanne I. Tuberculosis in patients receiving antiretroviral treatment: incidence, risk factors, and prevention strategies. J Acquir Immune DeficSyndr. 2011; 56:349–55.
39. World Health Organisation (WHO). Adherence to long term therapies: Evidence for action. WHO; 2010.Available from http://www.ijcm.org.in/www.who.int/chpt"_blank" www.who.int/chp/knowledge/publications/adherence_report/en/.
40. Achappa B, Madi D, Bhaskaran U, Ramapuram JT, Rao S, Mahalingam S. Adherence to antiretroviral therapy among people living with HIV. N Am J MedSci2013; 5:220-3
41. Uwakwe KA, Iwu AC, Diwe KC, Duru CB, Merenu IA. Socio-demographic determinants of compliance to scheduled clinic appointments among HIV patients in a Tertiary

Hospital in a Resource Limited Setting in Nigeria. Journal of Medical Education and Training 2017; 1:025.
42. Pawlowski A, Jansson M, Sköld M, Rottenberg ME, Källenius G (2012) Tuberculosis and HIV Co-Infection. PLoSPathog 8(2): e1002464. https://doi.org/10.1371/journal.ppat.1002464
43. Herbert, C., Luies, L., Loots, D.T. et al. The metabolic consequences of HIV/TB co-infection. BMC Infect Dis 23, 536 (2023). https://doi.org/10.1186/s12879-023-08505-4
44. Huante, M.B., Nusbaum, R.J., Endsley, J.J. (2019). Co-Infection with TB and HIV: Converging Epidemics, Clinical Challenges, and Microbial Synergy. In: Cirillo, J., Kong, Y. (eds) Tuberculosis Host-Pathogen Interactions. Springer, Cham. https://doi.org/10.1007/978-3-030-25381-3_7
45. Olivier, C., Luies, L. WHO Goals and Beyond: Managing HIV/TB Co-infection in South Africa. SN Compr. Clin. Med. 5, 251 (2023). https://doi.org/10.1007/s42399-023-01568-z
46. Zhou, Y., Li, T., Lin, S. et al. Characteristics and treatment outcomes of co-infected tuberculosis patients with human immunodeficiency virus in Southeast China, 2012–2021. BMC Infect Dis 23, 528 (2023). https://doi.org/10.1186/s12879-023-08501-8
47. Pawlowski A, Jansson M, Sköld M, Rottenberg ME, Källenius G (2012) Tuberculosis and HIV Co-Infection. PLoSPathog 8(2): e1002464. https://doi.org/10.1371/journal.ppat.1002464