



TUBERCULOSIS IN PATIENTS ATTENDING ART CENTRE AND ITS ASSOCIATION WITH CD4 COUNT

Medical Microbiology

**Dr. Sundaram
Supare**

Assistant Professor, GMC Nagpur

Dr. Sharmila Raut

Professor And Head Of The Department, IGMC Nagpur

Dr. Sonal Chavan

Associate Professor, GMC Nagpur.

Dr. Girish Patil

Assistant Professor, IGMC Nagpur

**Dr. Ravindra
Khadse**

Associate Professor, IGMC Nagpur

Dr. Anjali Patil

Associate Professor, IGMC Nagpur

ABSTRACT

Background HIV and tuberculosis (TB) are the most challenging infections faced by humanity and place immense burden on health care systems worldwide. Both HIV and TB impact one another's progression. HIV is the most important risk factor for progression of latent TB to active disease. TB is the most common cause of death among People Living with HIV (PLHIV). Timely detection of TB among PLHIV and screening for HIV among TB patients, early initiation of ART and ATT among coinfecting persons, provision of HIV-TB and other coinfections preventive therapy along with control of air-borne infection are some of the key activities to reduce morbidity and mortality among coinfecting persons. **Methods and Material** The study is a retrospective analysis of patient's record at ICTC and ART centre in a tertiary care hospital at central India. Data over a period of 7 years from January 2015 to December 2021 was analyzed. HIV and CD4 testing was done using NACO guidelines and diagnosis of pulmonary and extra-pulmonary tuberculosis was done according to RNTCP guidelines. **Results** In this study, total 250472 HIV positive patients in ICTC were followed up for treatment in the ART center from January 2015 to December 2021. Of them, 10245 (4.09%) were diagnosed as presumptive tuberculosis and out of these presumptive TB positive cases 1067 (10.41%) were diagnosed for TB. **Conclusions** Active TB in patients with HIV infection is a sign of disease progression to AIDS. Earlier identification of persons with signs and symptoms of TB and provision of TB prevention and treatment in a safe environment with no risk of TB transmission are crucially needed. Furthermore, all patients newly diagnosed with tuberculosis (new case or recurrence) should be encouraged to accept HIV testing.

KEYWORDS

AFB smear, CD4 count, extrapulmonary, HIV, pulmonary, tuberculosis

INTRODUCTION

Tuberculosis is the most common opportunistic infection in HIV infected patients. It is estimated that 60-70% of HIV positive persons will develop tuberculosis in their lifetime.¹ HIV infection favors the progression of latent tuberculosis to active infection by suppressing the immune response. Exogenous infection can also occur as HIV-infected individuals fail to contain new infection. Tuberculosis can occur at any stage of HIV disease, and its manifestation depend largely on the degree of immunosuppression.²

In the early stages of HIV infection pulmonary involvement is most common; with progressive immunosuppression, extra pulmonary involvement presenting as lymphadenitis is most common.³ Other organs involved in tuberculosis with advanced HIV disease include central nervous system, soft tissue, bone marrow, liver and other viscera. Extra pulmonary tuberculosis (EPTB) which usually account for about 15–20 % of the total TB cases, is now being increasingly reported due to the rise in the HIV pandemic and better diagnostic facilities.⁴

The burden of HIV-TB co-infection is increasing in India. According to the *India TB Report 2019*, overall prevalence of tuberculosis in HIV infected persons is around 3.4%. TB is the leading cause of morbidity and mortality among People Living with HIV (PLHIV). This group is 21 times more likely to develop TB than persons without the HIV virus. TB-HIV co-infection results in higher mortality rates. Nearly 25 per cent of all deaths among PLHIV are estimated to be due to TB.⁵

The present study is therefore undertaken to determine the prevalence of TB cases among HIV/AIDS patients attending ART center and to determine the relationship between tuberculosis and the degree of immunosuppression as determined by CD4 count in our region representing Central India.

AIMS AND OBJECTIVES

1. To determine the Tuberculosis in patients attending ART centre.
2. To study the socio-demographic determinants in TB diagnosed

HIV positive patients.

3. To study the association of CD4 count with pulmonary and extra-pulmonary tuberculosis in seropositive patients.

MATERIALS AND METHODS

The study is a retrospective analysis of patient's record at ICTC and ART centre in a tertiary care hospital at central India. Data of all HIV positive patients on ART treatment over a period of 7 years from January 2015 to December 2021 was analyzed. HIV infection was diagnosed using three antigenically different rapid kits as per the national HIV testing policy (ELISA/ Rapid/Simple) and CD4 cell counts were determined by flow-cytometry technique using **Facs Count machine with Facscount™ reagents (Becton Dickinson, USA)** using NACO guidelines. ART was started for eligible patients and was guided by baseline and 6-monthly CD4 counts in accordance with the national ART guidelines. Diagnosis of pulmonary and extra-pulmonary tuberculosis was established by clinical, radiological, histopathological and microbiological examination according to RNTCP guidelines and antitubercular treatment was started.

Ethical clearance was duly obtained from the Institute Ethical Committee for conducting the study. Data obtained were compiled, tabulated and analyzed. Tables and charts were prepared using Microsoft Word, Excel and Graph pad prism version 8.02. Study variables were expressed as percentages.

RESULTS

In this study, total 250472 HIV positive patients in ICTC were followed up for treatment in the ART center from January 2015 to December 2021. Of them, 10245 (4.09%) were diagnosed as presumptive tuberculosis and out of these presumptive TB positive cases 1067 (10.41%) were diagnosed for TB. (Table 1).

Table no. 1

Table 1: Year wise prevalence of Tuberculosis in HIV positive patients			
YEAR	No. of presumptive TB patients attending ART centre	No. of patients diagnosed with TB	%
2015	1156	223	19.29

2016	1221	203	17.03
2017	1159	199	17.16
2018	996	160	16.06
2019	2032	133	6.54
2020	2420	67	2.76
2021	1261	82	6.5
TOTAL	10245	1067	10.41

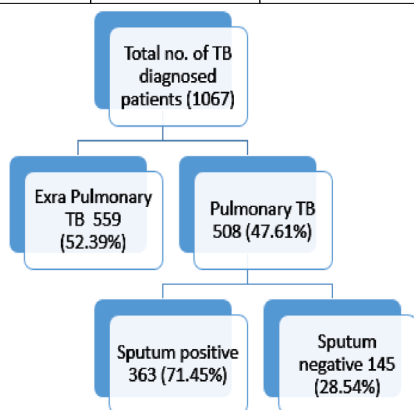


Figure 1: Pulmonary and extrapulmonary TB in HIV positive patients attending ART centre

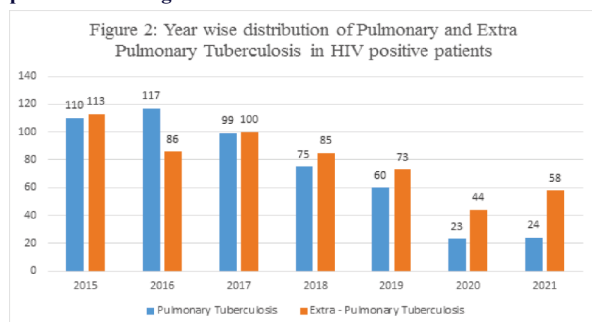


Figure no. 2

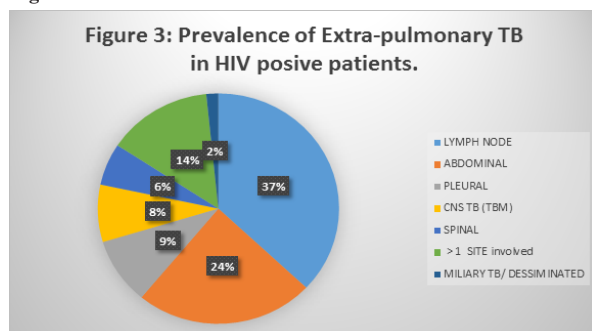


Figure no.3

Table no.2

Socio-demographic profile of HIV TB co-infected patients			
Parameter	Groups	Number	Percentage(%)
Age	0-20	23	2.15
	21-40	672	62.98
	41-60	298	27.92
	>60	74	6.93
Gender	Male	698	65.41
	Female	358	33.55
	Others	11	1.03
Residence	Urban	711	66.63
	Rural	356	33.36
Education	Illiterate	78	7.31
	Primary school	498	46.67
	Secondary school	354	33.17
	College and above	137	22.21

Table no.3

Marital status	Children <14 years	29	2.71
	Single	152	14.24
	Married	584	54.73
	Divorced / widow/ separated	262	24.55
	FSW	40	3.74
Occupation	Laborers	432	40.48
	Housewives	163	15.27
	Drivers	112	10.49
	Farmers	108	10.12
	Private Job	101	9.46
	Students/ unemployed	53	4.96

Table no.3

Association of Pulmonary and Extra-pulmonary Tuberculosis with CD4 count									
CD4 count	PTB (Sputum +)	PTB (Sputum -)	Lymph Node	Abdo -men	CNS/ TBM	Spinal	Pleur al	>1 site invol ved	Dissem inated / Milliar y TB
<100	142	77	102	68	22	-	22	59	9
101 - 200	43	59	31	13	-	-	18	20	-
201 - 300	78	12	28	21	10	-	13	-	-
301 - 400	11	7	8	4	-	3	3	-	-
401 - 500	5	3	8	6	-	23	4	-	-
>500	4	3	2	4	-	7	2	-	-
Total	363	145	207	134	45	33	52	79	9

DISCUSSION

Tuberculosis is the most common opportunistic infection in HIV-positive persons and may develop at any stage of the disease.⁶ In our study, total 250472 patients were tested positive for HIV in ICTC and followed up for treatment in the ART center from January 2015 to December 2021. Of them, 10245 (4.09%) were diagnosed as presumptive tuberculosis and out of these presumptive TB positive cases 1067 were diagnosed for TB. Table no.1 .

The present study shows that there is a sharp fall in detection of TB in 2019 (6.54%) and in 2020 (2.76%) as compared to previous years (Table 1). This could be an impact of Covid -19 pandemic suggests that detection and reporting of TB cases affected globally.¹²

In the present study, among the 1067 HIV- TB positive patients most of them were from the age group 21-40 years (62.98%) followed by 41 - 60 years (27.92%) living in urban area (66.33%) and majority of them were males (65.41%) (Table no.2). This group belongs to the economically productive and sexually active age group. Extremes of age were comparatively less affected. Similar study by kesari et al (2016)¹⁴ and Kamath *et al*¹ (2013) had reported that prevalence of HIV TB is more in sexually active age group (21-45 years) was 61.3%. Interestingly, married (54.73%) individuals were seen to have a higher rate of infection in comparison with single, divorced, or widowed individuals. This could be seen in light of the cultural drift toward the universality of marriage in the Indian context .¹⁵ The most Common occupation of the HIV/AIDS patients was labour work {40.48% (40% of males and 34.44% of females)}, house wife (15.27%), drivers (10.49%), farmer (10.20%). HIV had a tremendous impact on the livelihood of the affected individual as well as their family members.

As compared to immuno-competent individuals, the percentage of EPTB (Extra pulmonary tuberculosis) in HIV infected individuals is relatively high.¹⁶ EPTB still continues to pose several challenges in many areas. All EPTB patients should be considered potential pulmonary TB suspects unless coexisting pulmonary involvement is excluded. Documentation of EPTB in HIV is important because it constitutes an AIDS defining illness.¹⁷ EPTB occurs frequently and much earlier than other opportunistic infections in patients dually infected with HIV and TB as this infection can occur irrespective of any stage of HIV¹⁸

Findings of our study showed that extra pulmonary TB (52.38%) among HIV patients is little higher compared to pulmonary TB (47.61%) (Fig.1&2) . Ajay et al⁶ (57.47%) ,Sonam et al¹⁸ (69%) and Ragini Ghiya et al¹⁹ (68%) has shown similar findings , whereas lower rate of extra-pulmonary TB reported by Kesari et al¹⁴ (13.1%) and Jutang et al (38%)²⁰

Moreover, among pulmonary TB patients in HIV infected patients, 28.54% were smear negative (Fig1) . Paucibacillary nature of TB in PLHIV may lead to high proportion of smear negative TB patients.²¹

Extra pulmonary TB is the commonest cause of pyrexia of unknown origin (PUO) among HIV positive individuals in developing countries.²² The most frequent extra pulmonary form of TB is involvement of the lymph nodes with cervical region being the commonest. ² The commonest form of EPTB in our study group was lymph node tuberculosis diagnosed in 37 % patients followed by abdominal tuberculosis 24% ,pleural effusion 9% CNS 8%.(Fig.no.3) The study by Barthwal et al²⁴ shows lymph node 92% followed by other sites. Sonam et al¹⁸ has reported EPTB sites most common abdomen 72% followed peripheral LN 22%,pleural15%.

Unlike other opportunistic infections which have a selective range of CD4 in which the disease occurs, TB occurs throughout the course of HIV . The interaction between HIV and TB in persons coinfectd with HIV and TB is bidirectional and synergistic. Clinical presentation however depends on the level of immnuosuppression. Typical manifestations are frequent in early HIV and atypical features begin to occur as the immunity declines with more frequent extra pulmonary manifestations.²²

All the patients with disseminated tuberculosis had CD4 count below 200/cumm. This study showed that the prevalence of tuberculosis, both pulmonary and EPTB, in HIV-infected patients is higher with majority having CD4 cell count <100/cmm. Sputum positive pulmonary TB in 34% patients being highest no. compared to sputum negative cases with decreasing CD4 count.(Fig.no.3) Similar findings reported by ajay jaylal⁶ et al and Giri et al.²⁵

CONCLUSION

The present study found that most of the HIV infected patients were from sexually active age group. Standard of living and education maintain an increased frequency of TB in poor communities. Active TB in patients with HIV infection is a sign of disease progression to AIDS and is correlated with severe immunosuppression with low CD4 count and several cases of extrapulmonary TB. So , the study highlighted need of periodic screening of TB among HIV-infected individuals by the physicians treating HIV-infected patients in order to reduce the associated comorbidity resulting from the pairing of the infections. Furthermore, all patients newly diagnosed with tuberculosis (new case or recurrence) should be encouraged to accept HIV testing. Efforts should focus on early diagnosis of HIV infection with intensive health promotion strategy and early diagnosis of TB among HIV/AIDS people using higher sensitivity diagnostics.

REFERENCES:

- Swaminathan S, Ramachandran R, Bhaskar R, Ramanathan U, Prabhakar R, Datta M, et al. Development of tuberculosis in HIV infected individuals in India. *Int J Tuberc Lung Dis* 2000;4:839-44.
- Sharma SK, Mohan A, Kadiravan T. HIV-TB co-infection: a. Epidemiology, diagnosis and management. *Indian J Med Res* 2005;121:550-67.
- Pandit V, Valsalan R, Seshadri S, Bahuleyan S (2009) Disseminated tuberculosis presenting as mesenteric and cerebral abscess in HIV infection: case report. *Braz J Infect Dis* 13(5):383–386
- Shanmuganathan A, Shinivasan R, Thilagavathy G, Satish Kumar D, Sidduraj C et al (2013) Determination of sites involved, HIV co-infection and utility of diagnostic modalities in EPTB. *J Clin Diagn Res* 7(8):1644–1646
- India TB Report 2020. Revised National Tuberculosis Control Programme Annual Report. Central TB division. Ministry of health and family welfare.
- Jaryal A, Raina R, Sarkar M, Sharma A. Manifestations of tuberculosis in HIV/AIDS patients and its relationship with CD4 count. *Lung India* 2011;28:263-6.
- Mishra M, Bajare B, Shrikhande S. Retrospective study of HIV TB coinfection among patients attending ICTC in Nagpur ,Central India. *Global J for Research Analysis Dec.* 2020 : 9(12).
- Gunda DW, Kandala 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 northwestern Tanzania: a retrospective cohort study. *Can J Infect Dis Med Microbiol.* 2018;2018:1346104.
- Kamath R, Sharma V, Pattanshetty S, Hegde M B, Chandrasekaran V. HIV-TB coinfection: Clinico-epidemiological determinants at an antiretroviral therapy center in Southern India. *Lung India: official organ of Indian Chest Society* 2013; 30:302-306.
- Mishra S, Rukadikar A. Prevalence of pulmonary tuberculosis in HIV positive individuals. Its sensitivity and association with CD4 count. *Int.J. Curr. Microbiol. App. Sci* 2015;4(6):292-304
- Chavan VR, Chaudhary V., Ahir P. Current scenario of Opportunistic and coinfection in HIV –infected individuals at a tertiary care hospital in Mumbai, India. *IJMM* (2015) 339(1):78-83
- Alene KA, Wangdi K, Clements AC. Impact of the COVID-19 pandemic on tuberculosis control: an overview. *Tropical medicine and infectious disease.* 2020 Sep;5(3):123.
- Chakaya J, Khan M, Ntoumi F, Akililu E, Fatima R, Mwaba P, Kapata N, Mfinanga S, Hasnain SE, Katoto PD, Bulabula AN. Global Tuberculosis Report 2020–Reflections on the Global TB burden, treatment and prevention efforts. *International journal of infectious diseases.* 2021 Dec 1;113:S7-12.
- Kesari SP, Basnett B, Chettri A. Spectrum of Tuberculous Infection in Patients Suffering from HIV/AIDS and Its Correlation with CD-4 Counts: A Retrospective Study from Sikkim Indian J Otolaryngol Head Neck Surg (Apr–June 2019) 71(2):167–171;
- Gautam L, Deshpande J, Somasundaram K. Prevalence of hiv-tb co-infection, clinical profile and cd4 count of hiv patients attending art centre of ahmednagar, maharashtra International J of Medical Science and Public Health, 2014 : 3 (9)
- Chauhan T., Bhardwaj A., Parashar A. A study of an association between tuberculosis and HIV among ICTC attendees at a tertiary care hospital of Shimla, Himachal Pradesh, India. *IJHAS Jul-Sep 2012; 1(3):142-146*
- Shanmuganathan A, James B. Determination of Sites Involved, HIV Co-Infection & Utility of Diagnostic Modalities in EPTB. *J Clin Diagn Res.* 2013 Aug;7(8):1644-6.
- Spalgais S, Jaiswal A, Puri M, Sarin R, Agarwal U. Clinical profile and diagnosis of extrapulmonary tb in HIV infected patients: routine abdominal ultrasonography increases detection of abdominal tuberculosis. *The Indian Journal of Tuberculosis.* 2013 Jul;60(3):147-153.
- Ghiya R, Naik E, Beata C, Izurieta R, Marfatia Y. Clinico-Epidemiological profile of HIV/TB coinfectd patients in Vadodara, Gujarat. *Indian J Sex Transm Dis.* 2009; 30:10–15.
- Jutang Tiewsoh JB, Antony B, Boloor R. HIV-TB co-infection with clinical presentation, diagnosis, treatment, outcome and its relation to CD4 count, a cross-sectional study in a tertiary care hospital in coastal Karnataka. *J Family Med Prim Care* 2020;9:1160-5
- Kapadiya DJ, Dave PV, Vadera B, Patel PG, Chawla S, Saxena D. Assessment of tuberculosis prevalence in newly diagnosed human immunodeficiency virus-infected adults attending care and treatment center in Gujarat, India. *Indian J Community Med* 2018;43:185-9.
- Saunmya Swaminathan S and Narendran G 2008 HIV and tuberculosis in India; *J. Biosci.* 33 527–537
- Sharma SK, Agarwal G, Seth P, Saha PK. Increasing seropositivity among adult tuberculosis patients in Delhi. *Indian J Med Res* 2003;117:239-42.
- Barthwal MS, Rajan KE, Deoskar RB, Sharma SK. Extrapulmonary Tuberculosis in Human Immunodeficiency Virus Infection. *Med J Armed Forces India.* 2005 Oct;61(4):340-1.
- Giri PA, Deshpande JD, Phalke DB. Prevalence of pulmonary tuberculosis among HIV positive patients attending antiretroviral therapy clinic. *North Am J Med Sci* 2013;5:367-70.