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Original Research Article

Assessment of HIV-TB co-infection in newly diagnosed HIV positive patients and their correlation with CD4 and viral load

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ABSTRACT

Background: Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) constitute a major burden of infectious diseases in India. TB is the most common opportunistic infection and a leading cause of death among HIV positive patients. This study was conducted to assess the HIV–TB co-infection in newly diagnosed HIV patients and correlate co-infection with CD4 and viral load (VL).
Methods: A prospective observational study was carried out from January 2021 to June 2022 at ART center of a tertiary care hospital. Screening for TB was done by GeneXpert and Radiology. These patients were monitored for absolute CD4 count by flow cytometer and VL by Real time PCR.
Results: Among 380 newly diagnosed HIV patients screened, 94 (24.70%) had HIV-TB coinfection. Of these, 42 (44.6%) were pulmonary tuberculosis (PTB) and 52 (55.3%) were extrapulmonary tuberculosis (EPTB) of 42 patients with PTB, 31 (73.80%) were microbiologically confirmed by GeneXpert whereas of 52 patients with EPTB, 33 (63.46%) were diagnosed clinically and radio-logically. Of 94 patients, only 55 patients could be followed up further at 6 months. Of 55 patients, 33 (60%) had CD4 count <350 cells/mm^3 and 2 (3.6%) had baseline VL≥1000 copies/ml. 46.80% patients completed their anti-tubercular treatment.
Conclusions: EPTB was more as compared to PTB. Co-infection was more with low CD4 counts. Hence, CD4 test can be used as a good immunological marker in co-infection. The study highlights the need of periodic screening of newly diagnosed HIV patients for TB and their monitoring for CD4 and VL.

Keywords: HIV, TB, CD4, VL, GeneXpert

INTRODUCTION

HIV infection is one of the most common health problems all over the world affecting approximately 38 million people.[1] HIV infection has become a manageable chronic health condition because of increased access to efficient HIV prevention and treatment, including for opportunistic infections.[2,3] Despite all efforts made to combat the infection, it still constitutes a major burden of infectious diseases in developing countries like India. As per UNAIDS report 2021, it has been estimated that there are 38.4 million people living with HIV.1 In 2021, newly diagnosed HIV positive people were 1.5 million of which 63,000 people were reported in India.[1,4]

Tuberculosis (TB) is the most common serious opportunistic infection and leading cause of death among people with HIV infection all over the world.[5] HIV and TB are considered as the double burden diseases of the world.[6] As per global TB report 2021, in India 53,000 patients were reported to have TB in HIV positive patients. HIV-TB coinfection rate was 3.8%.

Approximately 11,000 patients died due to HIV- TB coinfection.[7] In India, people living with HIV (PLHIV) had a 20 fold higher risk of developing TB than those without HIV.[8] High death rates (15–18%) have been reported among HIV- infected TB cases.[9] HIV infection weakens the immune system and increases the risk of reactivation of latent TB infection into progressive primary TB disease and later endogenous reinfection of TB disease.[10,11] TB favours early viral replication and dissemination and contributes in progression of HIV disease to AIDS.[12] This results in long-lasting immune suppression, an increase in viral load or treatment failure of ART.[13] Though TB may occur at any stage of immunosuppression, risk of development of TB increases with depletion of CD4 count.[14] TB presentations in HIV-positive patients can vary depending on the degree of immunological suppression. Unusual clinical presentation and atypical radiological findings can result in missed or delayed diagnosis.[15] Thus, TB increases the morbidity and mortality associated with HIV.[12] HIV- TB co-infection places a diagnostic and therapeutic challenge in health care settings.[16] Thus, HIV-TB collaborative activities recommends intensified TB case findings at Integrated HIV counselling and testing centers (ICTCs) and antiretroviral therapy (ART) Centers.[17]

Early detection of TB infection in HIV and prompt initiation of TB treatment helps to reduce the mortality rate in HIV patients due to co-infection with TB.[18]

Thus, the present study was aimed to assess HIV-TB coinfection in newly diagnosed HIV positive patients and to corelate HIV-TB coinfection with CD4 and viral load.

METHODS

A prospective observational study was conducted in State Reference Laboratory, Department of Microbiology at a tertiary care hospital, Mumbai. The study was carried out over a period of 18 months from January 2021 to June 2022.

The details of the study were presented and approved by the Institutional Ethics Committee of Grant Government Medical College and Sir JJ Hospital, Mumbai. Informed consent was taken from all patients involved in the study.

A total of 380 newly diagnosed HIV positive patients enrolled at ART Center, Sir JJ Hospital, Mumbai were included in the study from January 2021 to December 2021. The patients were followed up at baseline and at 6 months for CD4 testing and at 6 months Viral load testing. Only newly diagnosed HIV-1 positive patients, more than 18 years and consenting to the study were included. Pregnant women, HIV-2 patients and patients not consenting were excluded from the study.

All newly diagnosed HIV positive patients after registration at ART center were evaluated clinically and underwent screening for TB along with a CD4+T lymphocyte count as a baseline investigation. Viral load testing was done after 6 months of ART initiation as per NACO guidelines. TB screening was done clinically by assessing the patient for signs and symptoms and radiologically by X-ray/ultrasonoFigurey. For TB confirmation, sputum sample was collected and processed by GeneXpert MTB/RIF assay. Blood sample of each patient was collected in two separate ethylene diamine tetra acetic acid (EDTA) tubes and was used for measurement of CD4+ T-cells count and viral load test. Absolute CD4+T cell count was done on whole blood with the Sysmex CyFlow Counter flow Cytometer and viral load testing was done on plasma sample using Abbott Real Time HIV 1 PCR Assay.

Statistical analysis

The statistical analysis was done using Statistical Package for the Social Sciences (SPSS) (Version 20.0.) Descriptive statistics and Wilcoxon Signed Rank Test were performed.

RESULTS

A total of 380 newly diagnosed HIV positive patients registered at ART center of Sir JJ Hospital, Mumbai were included in the study. Out of 380 patients, 94 HIV positive patients were found to be co-infected with tuberculosis during follow-up. Thus, HIV-TB coinfection rate was 24.7%. These 94 HIV- TB coinfected patients were followed up after 6 months for CD4 count and viral load assay. The results of these 94 HIV-TB coinfected patients was as follows:

Of total 94 HIV-TB coinfected patients, 59(62.7%) were male and 35(37.2%) were female (Figure 1).

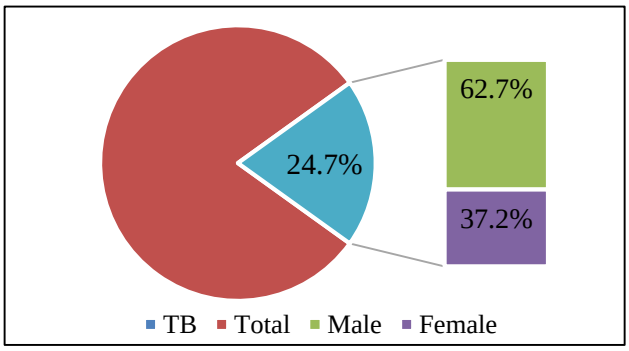

Figure 1: HIV-TB coinfection.

The most common affected age group was 46-60 years (44.68%) followed by 31-45 years (34.04%). Patients of age group > 60 years were least affected (2.32%). (Figure 2) Mean±SD age of HIV-TB coinfected patient was found to be 43.59±11.44.

Of the 94 HIV-TB coinfected patients, 42 (44.68%) patients had pulmonary tuberculosis whereas, 52 (55.31%) patients had extrapulmonary tuberculosis. Of

52 patients who had extrapulmonary tuberculosis, the most common manifestation was cervical lymphadenopathy (23%) and pleural effusion (23%) followed by abdominal lymphadenopathy (19.23%). (Table1).

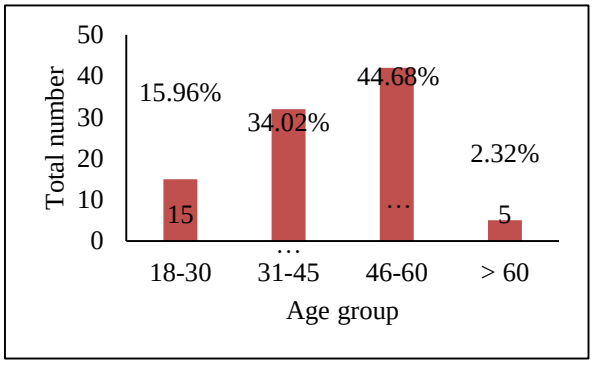

Figure 2: Age-wise distribution.

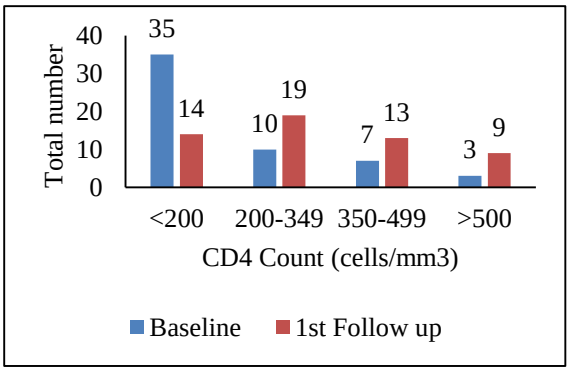

Figure 3: HIV-TB coinfection in correlation with immunological marker-CD4.

Diagnosis of tuberculosis was done microbiologically and radiologically. Microbiological diagnosis was done by GeneXpert and radiological diagnosis by Xray/USG. Of 94 patients, in 43 (46%) patients, tuberculosis was diagnosed by GeneXpert and in 39 (41%) patients, by radiology. In 12 (13%) patients, tuberculosis was diagnosed by both GeneXpert and radiology. Diagnosis of tuberculosis was done microbiologically and radiologically. Microbiological diagnosis was done by GeneXpert and radiological diagnosis by Xray/USG. Of 94 patients, in 43(46%) patients, tuberculosis was diagnosed by GeneXpert and in 39 (41%) patients, by radiology. In 12 (13%) patients, tuberculosis was diagnosed by both GeneXpert and radiology.

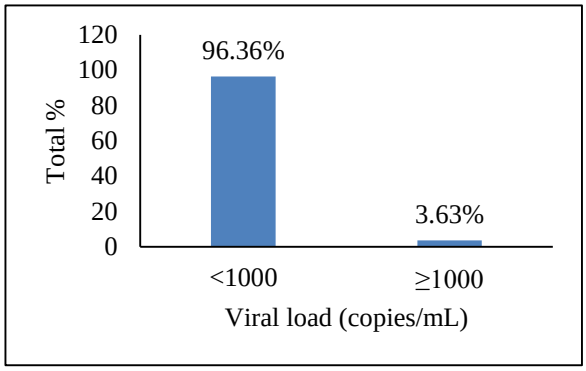

Figure 4: HIV-TB coinfection in correlation with virological marker-VL.

Table 1: Clinical manifestations of Extrapulmonary tuberculosis.

Presentation	Total	%
Cervical lymphadenopathy	12	23
Pleural effusion	12	23
Hepatosplenomegaly	8	15.38
Abdominal lymphadenopathy	10	19.23
Brain abscess	3	5.7
Tuberculoma	4	7.6
Others	3	5.7

Of the 42 pulmonary tuberculosis patients,31 patients were confirmed microbiologically, 6 were confirmed radiologically and 5 patients were confirmed both radiologically and microbiologically. Of 52 extrapulmonary tuberculosis patients, only 12 patients were confirmed microbiologically, whereas 33 patients were confirmed radiologically and 7 patients were confirmed both radiologically and microbiologically (Table 2). Of these 94 patients, 6 were found to be drug resistant tuberculosis and were confirmed microbiologically on GeneXpert MTB/RIF assay.

Table 2: Diagnosis of pulmonary and extrapulmonary tuberculosis.

Total pulmonary tuberculosis			Total extrapulmonary tuberculosis		
Diagnosis	**Cases**	**%**	**Diagnosis**	**Cases**	**%**
Microbiologically confirmed	31	73.80	Microbiologically confirmed	12	23.07
Radiologically confirmed	6	14.28	Radiologically confirmed	33	63.46
Both radiologically and microbiologically confirmed	5	11.90	Both radiologically and microbiologically confirmed	7	13.46
Total	42 (44.68)		**Total**	52 (55.31)	

Of these 6 MDR patients, 5 had pulmonary tuberculosis and 1 had extrapulmonary tuberculosis. Of total 94 patients, 19 patients were transferred out, 13 patients died and 7 patients were lost to follow up. Thus, only 55 patients were followed up for CD4 count and viral load assay after 6 months of antiretroviral therapy. Of 55

patients, 44 (46.8%) patients had completed antitubercular treatment and 11 patients were on anti-tubercular treatment. All 55 patients were on antiretroviral therapy. 55 HIV-TB coinfected patients were assessed for CD4 count at initiation of treatment. The mean CD4 count at baseline was 195.55 (median 150, range 25-971). At 6 months of ART initiation, it was observed that 14 patients had a CD4 count < 200 cells/mm3, 19 patients had a CD4 count between 200-349 cells/mm3 and 22 patients had a CD4 count of > 350 cells/mm3. (Figure 3). Thus, after 6 months of treatment the mean CD4 count improved to 335.27 (median 313, range 112-884).

Estimation of VL of these 55 patients showed that only 2 patients had VL ≥ 1000 copies/mL and 53 patients had VL < 1000 copies/mL (Figure 4).

DISCUSSION

In the present study, HIV-TB coinfection rate in newly diagnosed HIV positive patients was found to be 24.7%. A study conducted in Ethiopia by State Tesfaye B showed 25.6% HIV-TB co-infection which is close to the present study.[19] A study conducted in Gujarat by Kapadiya D et al have shown HIV-TB co-infection to be 17.8% and in Telangana by Reddy SG et al in 2016 to be 29.6%.[20,21]

Predominance was seen in males compared to females. Similar findings have been observed in a study conducted in Northern Tanzania by Edson W. Mollel et al in 2019 at Institute of Public Health.[22]

In the present study, most affected age group of HIV- TB confected patient was 46-60 years (44.68%). A study conducted by Dahiya et al reported maximum cases (60.60%) in age group of 25-34 years.[23] A study conducted by Aturaka et al reported 47.6% in the age group of 35-59 years.[24] Mean age group of the study population was 43.59 years which was in concordance with study conducted by Chandra et al (36.67 years).[25]

In the study, extrapulmonary tuberculosis was found in 55% patients as against 44% patients with pulmonary tuberculosis. A study conducted by Ameet Dravid et al, Private Health Care Centre, Pune have reported 73% of extrapulmonary tuberculosis.[26] In study conducted by Chandra NM et al, in Andhra Pradesh higher incidence of pulmonary tuberculosis (60%) has been reported as compared to extrapulmonary tuberculosis.[25]

In the present study, out of 94 HIV-TB coinfected patients, 5 patients had recurrence of tuberculosis which was approximately 5.31%. This finding was similar with the study conducted by Picon et al, who reported 5.95% TB recurrence.[27] Cause of recurrence could be exogenous reactivation or endogenous reinfection which cannot be distinguished from each other.

Most common site and clinical presentation of extrapulmonary tuberculosis was cervical lymphadenopathy and pleural effusion which was similar to a study conducted by Meghana M et al.[28]

In the present study, of 94 patients, 46% patients were diagnosed by GeneXpert, 41% radiologically, whereas 13% were diagnosed both by GeneXpert and radiology. A study conducted in Tanzania by Edson Mollel in 2019 also found higher utility of GeneXpert in diagnosis.[22]

Rifampicin resistance was reported in 6.38% patients and resistance was detected on GeneXpert MTB/RIF. GeneXpert proved to be a better diagnostic modality for pulmonary tuberculosis and drug resistance detection whereas, extrapulmonary tuberculosis was confirmed better radiologically.

Death rate in present study was 13.82% and maximum deaths were reported with depleted CD4 count. A study conducted by Kamath R et al however showed the death rate of 25%.[29] A favourable outcome of antitubercular treatment was seen in 46.80% of HIV-TB coinfected patients who have completed their treatment with regular medications.

In the present study, 55 patients were followed up at 6 months of TB diagnosis. It was observed that 63.63% patients had a baseline CD4 count of < 200 cells/mm3. Similar results of CD4 < 200 cells/mm3 were reported in the study conducted by Sidheshwari et al 60% and Chandwani et al 59.17% respectively. [30,31]

Our study suggests that risk of developing TB increases with depleted CD4 count in newly diagnosed HIV positive patients. After 6 months of follow up, the mean CD4 count was 335.27 cells/mm^3. A significant association by Wilcoxon Signed Rank Test was observed between CD4 count rise at 6 months and initial CD4 count (P value-0.00). Similar results were observed in the study conducted by Hegde MB in Udupi, South India.[29] Immunological improvement was observed after initiation of antiretroviral therapy and antitubercular treatment. In our study, the patients were followed up after 6 months for viral load, 96.36% patients responded well virologically and only 3.63% patients had a VL ≥1000 copies/mL. A study conducted by Temesgen Getaneh et al in Ethiopia have reported the prevalence of virological unsuppressed HIV-TB patients in Ethiopia at 39.09%.[32]

Limitations

Limitations of the study were HIV positive patients who diagnosed but not attended ART center for follow ups, conducted the study only on HIV-1 patients, paediatric patients, pregnant women and adolescents below 18 years were not included in the study, viral load testing was not done at baseline and the study was done over a period of 18 months only.

CONCLUSION

In newly diagnosed HIV positive patients, HIV-TB coinfection was found to be high. Thus, the study highlights need of periodic and frequent screening of tuberculosis in newly diagnosed HIV positive patients. Patients should be screened for tuberculosis by a molecular diagnostic technique along with clinical evaluation. Routine monitoring of HIV positive patients for CD4 and viral load is necessary, as a baseline CD4 count was found to be low in HIV-TB coinfected patients. HIV-TB coinfection and death rate was more with depleted CD4 count. CD4 count was thus found to be a good prognostic marker of tuberculosis coinfection than viral load assay. Immunological response found to be better with early initiation of antiretroviral therapy and antitubercular treatment.

Thus, all efforts should focus on early diagnosis of tuberculosis among HIV positive patients with intensive health promotion strategy and early initiation of antiretroviral therapy to prevent and treat tuberculosis in people living with HIV. Enhancement of TB infection control measures to prevent transmission of disease and management of both HIV and TB infections should be instituted to decrease morbidity and mortality among HIV infected persons.

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