Original Article

Clinico-Epidemiological Profile of TB Coinfection in HIV Positive Patients: A Hospital-Based Observational Study

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Abstract

Background: Tuberculosis (TB) remains the most common opportunistic infection among HIV-positive individuals and is a leading cause of morbidity and mortality worldwide. The interaction between TB and HIV significantly alters the clinical presentation, diagnosis, and outcomes of both diseases. The aim is to evaluate the clinico-epidemiological profile of TB coinfection in HIV-positive patients. **Material and Methods:** This observational study was conducted at a tertiary care center and included 250 HIV-positive patients diagnosed with tuberculosis. Data regarding demographic profile, clinical presentation, laboratory findings, type of TB, CD4 count, and treatment outcomes were collected and analyzed. **Results:** Among 250 HIV-positive patients, 70% had pulmonary TB, while 30% had extrapulmonary TB. The majority of patients were males (70.8%). The most affected age group was 31–45 years (50%) with Mean age of 38.85 years. Fever (67.6%), weight loss (6%), Anorexia (6.4%) and chronic cough (65.2%) were the most common symptoms. Patients with CD4 count <350 cells/mm³ showed a higher prevalence of extrapulmonary TB ($p<0.05$). Lymph node TB (28%) was the most common extrapulmonary manifestation. Treatment success rate was 78%, while mortality was observed in 12% of cases. **Conclusion:** TB coinfection in HIV patients shows a predominance of extrapulmonary involvement, especially in patients with low CD4 counts. Early diagnosis and integrated TB-HIV management strategies are essential to reduce morbidity and mortality.

Keywords: HIV, Tuberculosis, Coinfection, CD4 Count, Extrapulmonary TB.

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Introduction

Mycobacterium tuberculosis (MTB) is the causative agent of tuberculosis (TB), an airborne illness that typically affects the lungs and causes fever, chest aches, and severe coughing. Rising diabetes rates and persistently high rates of malnutrition are two factors contributing to TB vulnerability at the population level.[1] Although diabetes is becoming more common throughout the region, its negative effects on health are most noticeable in Pacific Island nations.[2] Lung health is seriously threatened by indoor and outdoor air pollution and cigarette smoking.[3] Additionally, they lower the possibility of a successful course of therapy and raise the risk of tuberculosis.[4] In 2013, an estimated five million new cases of tuberculosis were reported in the Asia-Pacific area, accounting for around 55% of the world's TB disease burden. Nearly all of the country's doctors deal with the rising morbidity and mortality rates caused by the two lethal diseases, HIV and TB. HIV/AIDS-related tuberculosis outbreaks in western nations are also a major factor in the global disease burden. For all TB patients, HIV testing is advised.[5] In 2014, the World Health Organization (WHO) projected that there are more than 9 million new active cases of tuberculosis, which leads to 1.5 million TB deaths annually. People who are HIV positive account for more than 25% of these fatalities.[6] The unique clinical picture of TB–HIV coinfection can make diagnosis and treatment difficult when both illnesses coexist in the same person.[7] Tuberculosis is one of the earliest opportunistic infections seen in HIV-infected individuals and is the leading cause of death in these patients.[8] TB–HIV coinfection has been reported to result in an accelerated course of disease and is also responsible for a disproportionately high number of TB-related deaths.[9-11] HIV-related immune suppression raises the possibility of latent TB reactivation and quick development to active infection. As a result, high HIV prevalence is also associated with high TB incidence rates.[8,9] According to the WHO data from 2014, over 80% of the 1.1 million TB patients who were HIV-positive were from Africa, indicating that TB–HIV coinfection is common in the continent.[6] Moreover, although a clear correlation has not yet been demonstrated, drug-resistant infections have been observed

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in TB–HIV coinfections.8 Thus, it is clear that efforts to prevent tuberculosis are adversely affected by HIV-related TB.

HIV-positive people are 29 times more likely than non-HIV people to develop active tuberculosis. According to WHO HIV-Associated Tuberculosis (2014), people with HIV are at a high risk of dying from multidrug-resistant and extensively drug-resistant TB. In March 2013, the National AIDS Control Organization reported that around 1.81 million persons living with HIV (PLHIV) were registered at Anti Retroviral Therapy (ART) Centers located throughout the nation. Guidelines for Antiretroviral Therapy for Adults and Adolescents Living with HIV (2013). According to the Central TB Division Training Module for Medical Practitioners (2010), tuberculosis is one of the main causes of death for people living with HIV/AIDS (PLHA) in India, where it affects 55–60% of AIDS patients. For the best possible patient care, collaborative tuberculosis and HIV initiatives are crucial for the prevention, diagnosis, and treatment of TB in individuals with HIV and HIV in TB patients (Harries, 1997). Collaborative TB and HIV initiatives, such as the diagnostic referral of suspected patients and closely monitored treatment regimens for both diseases, have been increasingly implemented worldwide in recent years.

Despite being treatable, tuberculosis is thought to be the leading cause of mortality for AIDS patients worldwide, accounting for at least 12% and possibly as much as 30–50% of all AIDS-related fatalities. Twelve TB and HIV create a kind of "disease complex" at the individual patient level, where each pathogen modifies the host response to increase the other pathogen's capacity to produce disease pathology. Mycobacterium typically infects the patient first, followed by HIV infection. There is a higher chance of latent TB infection reactivation, a higher chance of progressive TB disease from newly acquired TB infection, and an increased risk of recurrent TB or TB relapse with progressive HIV infection and its associated immune compromised state. When HIV infection precedes TB infection, such in the case of HIV transmission from mother to child, the generalised immunological suppression that follows secondary TB infection leads to drive.

In order to avoid mortality and morbidity, more research is now required in the fields of high-quality, integrated services for HIV and TB prevention, treatment, and care. So present study was conducted to study clinico-epidemiological profile of TB coinfection in HIV positive patients and to compare the occurrence of TB coinfection in HIV patients started on deferred ART regimen (CD4 guided) versus those started on early ART regimen (Regardless of CD4 count).

Materials and Methods

Hospital based cross sectional observational study was conducted among 250 HIV patients at Department of Medicine, SMS Medical College and Attached Hospital, Jaipur. Study was conducted from May 2019 to April 2020. Total sample size is calculated 242 patients of HIV – TB coinfection as per previous study showing prevalence of HIV-TB coinfection 18.6 for 80% power and a - error = 0.05 with absolute error = 5% (round off = 250 patients) as per seed article. This study was conducted on HIV patients attending department of medicine and ART centre, SMS Hospital, Jaipur. The patients was selected as per protocol based on inclusion and exclusion criteria till the desired sample size is attained. TB in HIV patients was diagnosed by clinical examination, sputum microscopy / CBNAAT with supportive evidence through HRCT chest, CSF study, pleural and ascitic fluid study. Data was collected by investigator himself and will be recorded on a predesigned study proforma. Ethical Clearance was obtained prior to the study from Institutional Research Review Board.

Inclusion Criteria

1. HIV positive OPD and IPD patients newly diagnosed with TB coinfection
2. Patients who have given written informed consent
3. Patients aged >18 years

Exclusion Criteria

1. HIV patients with old K-chest
2. Sick IPD patients having CD4 count <50 mm3

Statistical Analysis: The Statistical Package of Social Science (SPSS Version 26.0; Chicago Inc., USA) was used for statistical analysis. To determine the statistical significance of the comparisons, particular statistical tests were applied to the data. Mean values were used to compare quantitative variables, and proportions were used to compare qualitative ones. $P < 0.05$ was set as the significance level.

Results

The present Hospital based cross sectional observational study was conducted among 250 HIV patients at Department of Medicine, SMS Medical College and Attached Hospital, Jaipur. Here, majority (50%) of patients were in age group 31-45 years followed by 26.8% patients in age group 18-30years. Mean age was 38.85 years with standard deviation of 10.36. Here, this study was male dominant as 70.8% of patients were males and 29.2% of patients were females. According to our study, 62.4% patients were living in rural area and only 37.6% were living in urban area. [Table 1] Here, most of the patients had fever (67.6%), cough (65.2%) followed by SOB (6.8%), weight loss (6%), and Abdominal Pain (4%). [Table 2]

Here, 70% patients had Pulmonary TB while 30% patients had extra-Pulmonary TB. In our study, there were 95.2% TB-HIV patients with Respiratory system Involvement, 3.2% TB-HIV patients had GIT system involvement while 0.8% each of TB-HIV patients had CNS and CVS system involvement respectively. [Table 3]

According to our study, mostly patients (83.6%) had less than 350 CD4 Count at Time of HIV Diagnosis. In our study, mostly patients (85.2%) had less than 350 CD4 Count at Time of ART initiation. Here,89.2% patients had CD4 count less than 350 at the time of TB diagnosis while 10.8% patients had CD4 count more than or equal to 350 at Time of T.B. Diagnosis. [Table 4]

In our study,there were 29.2% patients of T.B. coinfection in HIV patients started on deferred ART regimen (CD4 guided) while 70.8% T.B.-HIV patients were those who started on early ART regimen (regardless of CD4 count). [Table 5]

In 38.4% of T.B.-HIV patients, MTB not detected,22.4% had no

expectoration while in 39.2% of T.B.-HIV patients, MTB detected 'R' sensitive. 60.8% patients were diagnosed by diagnostic methods other than CBNAAT in different fluids. [Table 6]

Table 1: Distribution of study subjects according to age & gender

Age Distribution (Years)	No. Of Patients	Percentage
18-30	67	26.8
31-45	125	50
46-60	48	19.2
61-75	10	4
Mean Age	38.85±10.36	
Gender		
Female	73	29.2
Male	177	70.8
Residential Area		
Rural	156	62.4
Urban	94	37.6
Total	250	100

Table 2: Distribution of Study Cases According to Clinical presentation (Chief Complains)

Chief Complaints	No. Of Patients	Percentage
Fever	169	67.6
Cough	163	65.2
SOB	17	6.8
Weight Loss	15	6
Abdominal Pain	10	4
Chest Pain	8	3.2
Anorexia	16	6.4
Asymptomatic	2	0.8
Back pain	4	1.6
Diarrhoea	2	0.8
Hemoptysis	3	1.2
Neck Pain	8	3.2
Dysuria	1	0.4
Burning Micturition	1	0.4
Altered sensorium	1	0.4
Headache	6	2.4
Weakness	2	0.8
Seizure	2	0.8
Axilla	1	0.4
Groin Pain	1	0.4
Testicular Pain	1	0.4

Table 3: Distribution According to System Involvement

TB	No. Of Patients	Percentage
Pulmonary TB	175	70
Extra-Pulmonary TB	75	30
Parameter		
TB patients with Respiratory System Involvement	238	95.2
TB patients with GIT system Abnormality	8	3.2
TB patients with CVS Abnormality	2	0.8
TB patients with CNS Abnormality	2	0.8

Table 4: Distribution according to cd4 count at the time of HIV diagnosis, At Time of ART initiation & At Time of T.B. Diagnosis

CD4 Count At Time Of HIV Diagnosis	No. Of Patients	Percentage
<350	209	83.6
≥350	41	16.4
CD4 Count At Time Of ART initiation	No. Of Patients	Percentage
<350	213	85.2
≥350	37	14.8
CD4 Count At Time Of T.B. Diagnosis	No. Of Patients	Percentage
<350	223	89.2
≥350	27	10.8

Table 5: Distribution according to art regardless of CD4 count

ART Regardless Of CD4 Count	No. Of Patients	Percentage
HIV patients started on deferred ART regimen(CD4 guided)	73	29.2
HIV patients started on early ART regimen(regardless of CD4 count)	177	70.8
Total	250	100

Table 6: distribution of study cases according to CBNAAT report

CBNAAT Report	No. Of Patients	Percentage
MTB not detected	96	38.4
MTB detected 'R' sensitive	98	39.2
No expectorant	56	22.4
Total	250	100

Discussion

The results of this one-year study showed that the HIV-affected group had a significant tuberculosis disease burden. The most common cause of patient death and morbidity is still tuberculosis. A total of 250 individuals were enrolled in our study, comprising all patients who visited our hospital's center and general medicine wards over the course of a year. Here, majority (50%) of patients were in age group 31-45 years followed by 26.8% patients in age group 18-30years. Mean age was 38.85 years with a standard deviation of 10.36. Prakash G O et al,[13] discovered that 40.75% of the participants were between the ages of 35 and 59. Chandwani et al. (35.61%), Aturaka et al. (47.6%), Said et al. (43%), and Kavya et al. (54%) all found similar results.[14-17] According to Dahiya et al., the 25–34 age range has the highest rate of HIV–TB co-infection (60.60%).[18] Prakash G O et al,[13] found the mean age to be 32 years which is comparable with our findings. Dahiya et al,[18] found mean age to be 31.18 years and Chandra et al found mean age as 36.67 years.[19]

Here, this study was male dominant as 70.8% of patients were males and 29.2% of patients were females. We found 80.8% patients were married, 13.25% were unmarried and 6% were widowed. Bariha P K et al,[20] found that among the 211 patients 174(82.68%) were males and 34 (16.45%) were females. 3(1.42%) revealed themselves as transsexuals. This shows a clear preponderance of male population in the disease cohort.[21] The studies in Manipur and Iran also showed that males are more affected than females.[22,23] But a study in Mumbai showed a marginal female majority as large number of female sex workers were included in that study.[24]

In our study 70% patients had Pulmonary TB while 30% patients had extra-Pulmonary TB. Kamath R et al,[25] found that 58.8% patients were of PTB and followed by EPTB in 38.2% patients. According to Unnikrishnan B et al26 around 50% of the co-infected cases were found to have extra-pulmonary tuberculosis (n=44).

We found that most of the patients had fever (67.6%), cough (65.2%) followed by SOB (6.8%), loss of appetite (6.4%), weight loss (6%), and Abdominal Pain (4%). Here according to our study, 40.8% patients were smokers, 32% patients were ethanol users while 6.4% were hypertensives on medication. In our study 12.6% patients had pallor and 7.6% had lymphadenopathy. According to a study by Bariha P K et al20 most of the patients with Pulmonary TB complained of cough (35%), weight loss (20%) and loss of appetite (22%) cases. Fever was seen in 11%, 13% cases had hemoptysis.[22] They found that most of the patients with EPTB had fever (6.72%), weight loss (8.40%) and loss of appetite (5.88%). Abdominal distension (5.88%) and diarrhea (6.72%) were the major symptoms in gastrointestinal TB, while cough (23.52%) and chest pain (5.04%) were the major symptoms in pleural TB. Gautam L et al found that the main clinical feature complained by HIV patients were fatigue (75.06%), weight loss (72.46%), fever (68.57%), oral ulcers (32.47%). Niraula et al (2013) found that 53.8% had fever, 46.5% experienced weight loss, 41% suffered from chronic diarrhea, 37.2% had cough, 23.6% used to get fatigue easily, 12.8% had oral lesions, 3.8% had genital lesions and 2.8% had night sweats. Other studies by Singh et al (2013) and Rao et al28 (2012) also had the similar findings.[26-29]

According to our study, mostly patients (83.6%) had less than 350 CD4 Count at Time of HIV Diagnosis. At Time of ART initiation mostly patients (85.2%) had less than 350 CD4 Count. At Time of T.B. Diagnosis, 89.2% patients had CD4 count less than 350 at the time of TB diagnosis while 10.8% patients had CD4 count more than or equal to 350. We also found that at the Time of HIV Diagnosis the mean CD4 count was 159.19 and 170.5 at Time of T.B. Diagnosis and 152.8 at Time of ART Initiation measured under less than 350 CD4 count. Prakash G O et al discovered that people living with HIV (PLHIV) are using CD4 cell count testing less to determine when to begin antiretroviral therapy (ART) and how to monitor treatment. ART can be initiated regardless of CD4 cell count, and for PLHIV who are stable on ART, CD4 cell count monitoring can be discontinued because viral load can be used to gauge ART effectiveness. CD4 cell count measurement is currently a crucial technique in the treatment of advanced HIV illness. The highest percentage of cases in our study (50.39%) had a CD4 cell count below 200 cells/µL. Chandwani et al., Yasmin et al., and Sidheshwari et al. research findings of 59.17%, 60.38%, and 60%, respectively, are correlated with our study results. This graph illustrates how patients with HIV have a higher risk of developing tuberculosis when their CD4 cell count declines. The average CD4 cell count among HIV-TB patients in our study was 227.6. This finding is consistent with findings by Dahiya et al.18 (199.0), Chandra et al,[19] (218.32), Kamath et al,[25] (147.47), Rajbhandari et al,[30] (123.70) and Singh PK (166.7).[31] TB is the most prevalent opportunistic infection among HIV-positive people with a CD4 cell count, according to Harshini N et al.[32]

In our study 70.8% HIV patients started on early ART regimen (regardless of CD4 count) and only 29.2% HIV patients started on deferred ART regimen (CD4 guided). Harshini N et al discovered that, of the 107 HIV/TB co-infected people, 54 (50.9%) were receiving pre-antiretroviral therapy (Pre-ART), 46 (42.9%) were receiving antiretroviral therapy (ART), and a small number had unknown treatment status. According to a Combodia study, the introduction of antiretroviral therapy reduced resistance to anti-tubercular medications from 48% in 1999 to 7.9% in 2004 (Sungkanuparph et al., 2007).[33]

In our study, in 38.4% of T.B.-HIV patients, MTB not detected, 22.4% had no expectoration while in 39.2% of T.B.-HIV patients, MTB detected 'R' sensitive meaning 60.8% patients were diagnosed by diagnostic methods other than CBNAAT in

different fluids. A study by Deivanayagam C N et al,[34] discovered that 618 individuals (61.8%) out of 1000 evaluated had culturable M. tuberculosis in their sputum sample. It was discovered that 49.5% of patients had expectorate tubercle bacilli that were resistant to one or more anti-TB medications. MDR-TB was found in 339 individuals (33.9%). 4.42% of MDR-TB patients tested positive for HIV. Sachdeva K et al,[35] revealed that 58.3% of the twelve individuals who underwent CBNAAT were positive for TB. Only 16.6% of this tested positive for tuberculosis when acid fast bacilli were examined under a microscope (ZN staining). There are very few Indian studies on CBNAAT. When CBNAAT was used to diagnose tuberculosis instead of fluorescence microscopy, research conducted in Hyderabad in 2011 revealed an incremental case detection of 10.8%.[36]

Conclusion

HIV-TB co-infection is a major public health concern, and HIV infection is the most powerful risk factor for tuberculosis. Low baseline CD4 cell counts (less than 350 cells/µL), patients' rural backgrounds, low levels of education, nutritional status, and sputum smear-positive pulmonary tuberculosis were identified to be independent risk factors for unfavourable outcomes. We advise those involved in managing HIV and TB to concentrate on these risk factors in light of these findings. Raising working-class and rural residents' understanding of the illness may be crucial to its early detection and prevention. To stop the simultaneous threat of the HIV-TB epidemic, persistent efforts are required to identify and cure tuberculosis in HIV-positive individuals, even though the trend of HIV-TB co-infection is declining.

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Conflicts of interest

There are no conflicts of interest.

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