



**ORIGINAL RESEARCH PAPER**

**Medicine**

**CLINICO-RADIOLOGICAL PRESENTATION OF PULMONARY TUBERCULOSIS IN HIV POSITIVE PATIENTS IN A TERTIARY CARE HOSPITAL OF EASTERN INDIA**

**KEY WORDS:** HIV, PTB, DR-TB, PLHWA

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**ABSTRACT**

**INTRODUCTION:** The deadliest combination of the two devastating and killer disease TB & HIV has been closely linked since the emergence of AIDS contributing the progress and pathogenecity of each other, and As half of the HIV patients are likely to be infected with tuberculosis, the twin challenge of this "CURSED DUET" seems to be daunting<sup>1</sup>. There has been increase rate of DR TB, MDR TB, XDR TB, which are difficult to treat and contribute to increase mortality. In a developing country like India, the potential extra burden of new tuberculosis cases attributable to HIV is staggering and could overwhelm the already stretched tuberculosis budgets and support services.

**AIMS & OBJECTIVES:** To study and co-relate clinical and radiological features of Pulmonary TB in HIV positive patients, comparison with degree of immunosuppression. To compare the CD<sub>4</sub> T-cell count and sputum status before and after ATT treatment completion.

**MATERIALS & METHODS:** This is a prospective cohort study conducted on 51 patients admitted to Department of Pulmonary Medicine, S.C.B. Medical College, Cuttack from September 2011 to august 2013. The patients included in the study were all TB patients of age >15 years with strong clinical suspicion of HIV/AIDS. Pulmonary TB was diagnosed either with sputum smear positive or Chest x-ray. When EPTB was suspected as a possible diagnosis, every attempt was made to procure tissue/relevant body fluid for diagnostic testing. Rapid tests are in vitro qualitative tests for the detection of antibodies to Human Immunodeficiency Virus(HIV) types 1 &2 in human serum, plasma, whole blood, urine, saliva was used for diagnosis of HIV. Patients with only extra Pulmonary Tuberculosis and no evidence of pulmonary tuberculosis and Patients with PCP, fungal infection and sepsis were not included because these conditions cause lymphopenia and decreases CD<sub>4</sub> T-cell count.

**RESULTS:** Out of these 51 patients, most of the HIV-TB co-infected patients (62.5%) were seen among sexually active age group of 25-44 yrs. 92% of the patients were male and 8% were females. Most frequently encountered symptoms were fever(78.5%), cough (72.5%), loss of appetite(68.5%) and loss of weight(66.5%). Most common non-respiratory sign was pallor (67%), oral thrush(21.5%), lymphadenopathy(17.5%) and most common respiratory sign was crepitations (49%). B/L involvement was seen in 55% cases. About 74.5% cases were moderately or far advanced disease on the chest radiograph. The typical radiological findings of post primary TB, i.e. upper zone infiltrate, fibrosis and cavities were found in 25%, 4% and 6% cases respectively. Pleural effusion was detected in 10%, pneumothorax in 2% and hydropneumothorax in 2% cases. In our case 33% of the patients had CD4 count 0-50, 27.5% had CD4 count 51-100, 19.5% had CD4 count 101-150, 12% had CD4 count 151-200 and only 8% had CD4 count above 200. Comparing CD4 count with radiological findings infiltration and military tuberculosis were distributed over all ranges of CD4 counts. Cavitory lesions were more in CD4 count above 100. Overall sputum positive PTB was 74.5% and sputum negative PTB was 25.5%. Treatment outcome in sputum positive patients were cured in 63%, death in 23.5%, failure in 8% and defaulter in 5.5%. In patients with sputum smear negative PTB treatment completed were 69.5%, death occurred in 15.5%, defaulter and failure was seen in 7.5% each.

**CONCLUSION:** Treatment of HIV-TB co infection requires strong commitment and a focused approach. A strong coordination between the national TB and AIDS control programmes is required for effective management of TB-HIV patients.

**INTRODUCTION:** According to WHO report 2007, south East Asia Region accounts for 18% of the world HIV infected patients and nearly 40% of all tuberculosis cases globally<sup>2</sup>. Recently released national HIV prevalence estimates for India indicate that 0.22% of women and 0.36% of men aged 15-49 years are infected<sup>3</sup>. **HIV pandemic fuels the TB epidemic:** - HIV infection has contributed to a significant increase in worldwide incidence of TB by producing a progressive decline in cell mediated immunity. HIV alters the pathogenecity of TB greatly leading to more frequent extra pulmonary involvement and atypical radiological manifestations. Worldwide, TB is most common opportunistic infection affecting HIV seropositive individuals and the most common cause of death in patients with AIDS. In developing countries TB accounts for about 1/3<sup>rd</sup> of all deaths and deadly synergy between HIV and TB is the leading cause of mortality among infectious disease in developing world. Factors like - malnutrition, overcrowding, unemployment, alcoholism, drug abuse, poverty and homelessness are responsible both for TB and HIV. Extra pulmonary TB, disseminated TB and sputum negative manifestations are more common in patients with advanced

immune-suppression. While TB prevalence has remained stable, TB incidence continues to rise especially in countries most severely affected by HIV epidemic. HIV promotes progression to active TB in patients with mycobacterium Tuberculosis infection. The life time risk of TB in immune competent person is 5-10%, but in HIV positive, it is 5-15% per year. Without proper treatment 90% of the people living with HIV die within 6-24 months of contracting TB<sup>4</sup>. HIV in TB patients lead to low cure rate, high morbidity and mortality during treatment, high defaulter rates because of adverse drug reactions, high recurrence rates and increased transmission of drug resistant strains among HIV-infected patients in congregate settings<sup>5</sup>. TB affects HIV ; as TB shortens the survival of patients with HIV infection, accelerates the progression of HIV by increasing viral load and late TB diagnosis contributes to increased death rates in PLWHA<sup>5</sup>. HIV per se does not appear to be predisposing factor for MDR-TB but HIV with TB increases MDR TB by defaulting of patients due to drug interaction and toxicities, malabsorption to ATT due to gastroenteropathies, increased frequency of visit to hospital and exposure to MDR TB patients<sup>6</sup>.

A wide clinicoradiological spectrum of tuberculosis was seen among HIV patients, in consonance with their varying immune status. With the conventional sputum test not providing an adequate diagnostic help, familiarity with the clinicoradiological spectrum of tuberculosis and coexisting opportunistic infections is absolutely necessary. This study makes an attempt to correlate the clinical presentation, chest X-ray and CD4 counts, as it will help in better understanding this deadly duo of HIV and tuberculosis.

**AIM & OBJECTIVES:**

- 1) To study and co-relate the clinical manifestations and radiological patterns of Pulmonary TB in HIV positive patients.
- 2) To co-relate various clinical and radiological manifestations of Pulmonary TB patients with degree of immunosuppression as evidenced by CD<sub>4</sub> T-cell counts in HIV positive patients.
- 3) To compare the CD<sub>4</sub> T-cell count and sputum status before and after ATT treatment completion.
- 4) To assess the treatment outcomes

**MATERIALS AND METHODS:** Confidentiality of the data collected was maintained. Written consent was taken from the patient to be a part of the study. The present study was done as a prospective cohort study in a tertiary care hospital of East India(Dept. of Pulmonary Medicine, S.C.B. Medical College, Cuttack) from September 2011 to august 2013. 47 HIV-positive male patients and 4 HIV-positive females, who satisfy the inclusion criteria, were the subjects of the study. All patients above the age of 12 with confirmed HIV infection as per NACO guidelines were the subjects of the study. After pretest counseling and informed consent, anti- HIV antibody tests were performed (as per the NACO guidelines) by the rapid tests (COMB-AIDS RS kit, and If positive the results were confirmed using the NEVA-HIV and VIRADOT KIT).

These individuals were subsequently assessed thoroughly as per the protocol. This included detailed clinical history including presenting symptoms, past history, disease diagnosis, and complete physical examination followed by appropriate laboratory tests. The chest radiography was taken for all the patients and detailed evaluation of the radiograph was done. CD4 count was estimated at the same point of time. Sputum AFB stain was carried out to look for pulmonary tuberculosis. When EPTB is suspected as a possible diagnosis, every attempt should be made to procure tissue/relevant body fluid for diagnostic testing. Most accessible tissue should be procured for histopathological, cytopathological and microbiological diagnosis. USG Thorax / Abdomen / Pelvis, CT THORAX/ HRCT were carried out in specific cases, where required.

**RESULTS:** Most of the HIV-TB co-infected patients (62.5%) were seen among sexually active age group of 25-44 yrs. 92% of the patients were male and 8% were females. 80.5% of the patients were married and 19.5% were unmarried. Most of our patients were labourers (33%) followed by drivers (25.5%). Migration history to metropolis or industrial town to earn their livelihood was present in 65% of the patients. 84% of the cases had some form of addiction. Out of which smoking was commonest (61%), alcohol (53%) followed by tobacco chewing (31%).

Most frequently encountered symptoms were fever(78.5%), cough (72.5%), loss of appetite(68.5%) and loss of weight(66.5%).Most common non-respiratory sign was pallor (67%), oral thrush(21.5%), lymphadenopathy(17.5%) and most common respiratory sign was crepitations (49%).

On the chest radiograph, B/L involvement was seen in 55% cases. About 74.5% cases were moderately or far advanced disease. The typical radiological findings of post primary TB, i.e. upper zone infiltrate, fibrosis and cavities were found in 25%, 4% and 6% cases respectively. Atypical features such as middle and lower zone infiltrates, consolidation and intra thoracic lymphadenopathy were found in 35%, 2% and 8% cases respectively. Infiltrates over all zones were found in 10% cases while miliary shadows were present in 8% cases. Pleural effusion was detected in 10%, pneumothorax in 2% and hydropneumothorax in 2% cases.

FNAC suggestive of TB lymphadenitis in 10% cases. Pleural fluid suggestive of tubercular in origin in 10% cases, ascitic fluid 4% and CSF in 2% cases.

In our case 33% of the patients had CD4 count 0-50, 27.5% had CD4 count 51-100, 19.5% had CD4 count 101-150, 12% had CD4 count 151-200 and only 8% had CD4 count above 200.

Overall incidence of EPTB along with PTB in our study were 37%, among them 42% had CD4 count 0-50, 21% had CD4 count 51-100 and rest 37% had CD4 above 100 indicating EPTB were more common in advanced stage of the disease.

Comparing CD4 count with radiological findings infiltration and military tuberculosis were distributed over all ranges of CD4 counts. Cavitory lesions were more in CD4 count above 100.

Overall sputum positive PTB was 74.5% and sputum negative PTB was 25.5%. Both positive and negative sputum status was present in all the CD4 ranges.

Treatment outcome in sputum positive patients were cured in 63%, death in 23.5%, failure in 8% and defaulter in 5.5%. In patients with sputum smear negative PTB treatment completed were 69.5%, death occurred in 15.5%, defaulter and failure was seen in 7.5% each.

Correlation of CD4 count with treatment outcome showed that cured and treatment completed patients were more in CD4 count above 50(78.5% for CD4 count 51-100, 70% for CD4 count 101-150, 66% for CD4 count 151-200 and 75% for CD4 count above 200) and less in CD4 count below 50(47%). Similarly deaths were more in CD4 count below 50(29%) and less in CD4 count above 50(14.5% for CD4 count 51-100, 20% for CD4 count 101-150, 17% for CD4 count 151-200).

CD4 count after treatment completion showed patient who got cured/completed the treatment had CD4 count increased in 85% cases where as patient who declared failure CD4 count increased in only 15% cases .Among patients with increased CD4 count mean change in CD4 count was from 120 before treatment initiation to 281 after treatment completion similarly among patients with decreased CD4 count mean change was from 82 to 67. So overall change in mean CD4 count was 113 before treatment initiation to 241 after treatment completion.

Treatment outcome in sputum positive patients were cured in 63%, death in 23.5%, failure in 8% and defaulter in 5.5%. In patients with sputum smear negative PTB treatment completed were 69.5%, death occurred in 15.5%, defaulter and failure was seen in 7.5% each. Correlation of CD4 count with treatment outcome showed that cured and treatment completed patients were more in CD4 count above 50(78.5% for CD4 count 51-100, 70% for CD4 count 101-150, 66% for CD4 count 151-200 and 75% for CD4 count above 200) and less in CD4 count below 50(47%). Similarly deaths were more in CD4 count below 50(29%) and less in CD4 count above 50(14.5% for CD4 count 51-100, 20% for CD4 count 101-150, 17% for CD4 count 151-200).

**DISTRIBUTION OF CLINICAL SYMPTOMS IN HIV-TB CO-INFECTED PATIENTS (N=51)**

SYMPTOMS	NO OF PATIENTS	% OF PATIENTS
Fever	40	78.5%
Cough	37	72.5%
Haemoptysis	19	37.5%
Chest pain	10	20%
Breathlessness	25	49%
Loss of appetite	35	68.5%
Loss of weight	34	66.5%
Night sweats	24	47%
Diarrhoea	13	25.5%
Odynophagia	10	20%

Malaise	23	45%
Abdominal pain	7	14%
Headache	8	15.5%
Disorientation	4	8%

**DISTRIBUTION OF CLINICAL SIGNS IN HIV-TB CO-INFECTED PATIENTS(n=51)**

CLINICAL SIGNS	NO OF PATIENTS	% OF PATIENTS
Pallor	34	67%
Cyanosis	3	6%
Pedal oedema	8	15.5%
Clubbing	10	19.5%
Lymphadenopathy	9	17.5%
Oral thrush	11	21.5%
Jaundice	4	8%

**DISTRIBUTION OF CD4 T LYMPHOCYTE CELLS IN HIV-TB CO-INFECTED PATIENTS (n=51)**

Cd4 COUNT	NO OF PATIENTS	% OF PATIENTS
0-50	17	33%
51-100	14	27.5%
101-150	10	19.5%
151-200	6	12%
GREATER THAN 200	4	8%

**RADIOLOGICAL EXTENT OF PTB IN HIV-TB CO-INFECTED PATIENTS (n=51)**

RADIOLOGICAL EXTENT	NO OF PATIENTS	% OF PATIENTS
Bilateral	28	55%
Unilateral	23	45%
Minimal	13	25.5%
Moderately advanced	29	57%
Far Advanced	9	17.5%

**ZONEWISE DISTRIBUTION OF PTB IN HIV-TB CO-INFECTED PATIENTS (n=51)**

PREDOMINANT LESION	TYPE OF LESION	NO OF PATIENTS	% OF PATIENTS
Upper zone	INFILTRATION	13	25%
	FIBROSIS	2	4%
	CAVITATION	3	6%
	CONSOLIDATION	1	2%
Mid and lower zone	INFILTRATION	18	35%
	FIBROSIS	2	4%
	CAVITATION	2	4%
	CONSOLIDATION	1	2%
All zone	INFILTRATION	5	10%
	MILIARY	4	8%

**CORRELATION OF RADIOGRAPHIC FINDINGS WITH CD4 COUNT (n=51)**

TYPE OF LESION	Cd4 0-50	CD4 51-100	CD4 101-150	CD4 151-200	CD4 >200
INFILTRATION	13 (76.5%)	11 (79%)	7 (70%)	3 (50%)	2 (50%)
CAVITY FIBROSIS	1(6%)	1(7%)	2(20%) 1(10%)	1(16.6%) 1(16.6%)	1(25%) 1(25%)
CONSOLIDATION	1(6%)	1(7%)			
MILIARY	2 (11.5%)	1(7%)		1(16.6%)	
PLEURAL EFFUSION	2 (11.5%)	1(7%)	1(10%)	1(16.6%)	
HILAR LYMPH NODE	1 (6%)	2(14%)	1(10%)		

**PRESENTATION OF EPTB ACCORDING TO CD4 COUNT IN HIV-TB CO-INFECTED PATIENTS (n=19)**

CD4 CELL COUNT	NO OF EPTB PATIENTS	% OF EPTB PATIENTS
0-50	8	42%
51-100	4	21%
101-150	5	26%
151-200	1	5.5%
>200	1	5.5%

**CORRELATION OF SPUTUM STATUS WITH CD4 COUNT IN HIV-TB CO-INFECTED PATIENTS (n=51)**

Cd4 COUNT	SPUTUM POSITIVE (n=38=74.5%)	SPUTUM NEGATIVE (n=13=25.5%)
0-50	12(70.5%)	5(29.5%)
51-100	11(78.5%)	3(21.5%)
101-150	8(80%)	2(20%)
151-200	4(66.5%)	2(33.5%)
GREATER THAN 200	3(75%)	1(25%)

**DISCUSSION:** Tuberculosis, unlike other HIV-associated opportunistic infections, may occur at relatively high levels of CD4 counts, although its frequency markedly increases in patients with more severe immunosuppression HIV-TB cases have been observed to have severe immunosuppression at presentation.

Most patients of our study were belonged to age group 35-45yrs (43%) followed by 25-34yrs (25.5%) together constituting about 69% of the patients. Our study is in accordance with the studies by S Bhagyabati et al<sup>6</sup> found 63% and C N Devianagayam et al<sup>7</sup> found 75%, Asmita A et al<sup>8</sup> found 76% subjects in sexually active group. Of all patients of our study 47(92%) were males and 4(8%) were females. Similar study has been reported in other studies in India (S Bhagyabati Devi et al<sup>6</sup>, C N Devianagayam<sup>7</sup>, SwaminathanS et al<sup>9</sup>, Asmita A et al<sup>8</sup>).

Out of 51 patients, most frequently encountered symptoms were fever (78.5%), cough (72.5%), loss of appetite (68.5%) and loss of weight (66.5%). malaise was present in 45% cases, breathlessness in 49%, night sweat in 47%, haemoptysis in 37.5%, diarrhoea in 25%, chest pain 29%, odynophagia in 17.5%. This is again consistent with most of the studies; e.g Zuber Ahmad et al<sup>10</sup>, S Bhagyabati Devi et al<sup>6</sup>, K C Mohanty et al<sup>11</sup>, C N Devianagayam et al<sup>7</sup> and P Kumar et al<sup>12</sup> reported similar profile. Signs noted on general examination showed pallor was commonest (67%), oral thrush in (21.5%), clubbing (19.5%), lymphadenopathy in 17.5%, pedal oedema in 15.5% and jaundice in 8% cases. Among respiratory signs bronchial BS in 17.5% cases, crepitations in 49% cases and rhonci in 21% cases. SwaminathanS et al<sup>9</sup> found clubbing in 18%, oral thrush in 38%, lymphadenopathy in 29% and crepitations in 55%. Kumar P et al<sup>12</sup> found peripheral lymphadenopathy in 11.9% and oral thrush in 28.6%. Pallor was the most noticeable signs in our study because large numbers of patients were in advanced stage of the disease.

CD4 count of 0-50 was present in 42% cases, 51-100 in 21% cases and 101-150 in 26% cases and only 11% had CD4 count more than 200. S Swaminathan et al<sup>9</sup> found risk of tuberculosis in HIV-TB co-infection increases when CD4 count falls. On comparison of different radiological manifestations with CD4 count infiltration was present in almost all ranges i.e 70-80% cases with CD4 count <150 and 50% cases with CD4 count >150. Cavity seen in <10% cases with CD4 count <100 and 15-25% with CD4 100 same for fibrosis. Consolidation is seen in CD4 count less than 100. Miliary tuberculosis mainly seen in CD4 count less than 50, i.e. out of 4 cases 2 were found in this range. PLEF also mainly seen in CD4 count less than 50, i.e. out of 5 cases 2 were found in this range. This showed greater is degree of immunosuppression more is the atypical presentation.

On analysing sites of involvement of EPTB in PTB 17.5% cases had lymph node among which 10% cases found to be tubercular in FNAC( 80% in cervical area and 10% in supraclavicular area) , 10% had PLEF, 2% cases of pneumothorax, 2% cases of hydropneumothorax, 2% cases of TB meningitis, 4% cases of TB abdomen. Overall involvement of EPTB in PTB is 37%. Kumar P et

al<sup>12</sup> and Swaminathan S et al<sup>9</sup> found 45.6% and 30% of their patients to have concomitant EPTB respectively with lymph node affection being the commonest site of involvement. Kumar P et al<sup>12</sup> found 11.9% and 6.85% of the patients had intra and extra thoracic lymphadenopathy respectively and pleural involvement was in 9.5% cases.

Sputum was positive in 74.5% cases and negative in 25.5% cases overall. In between CD4 count 0-50 it was positive in 70.5% and negative in 29.5% cases, in between 51-100 it was positive in 78.5%, in between 101-150 it was positive in 80%, in between 151-200 it was positive in 66.5% and >200 count it was positive in 75% cases. Thus in this study it was seen, despite having very low CD4 count, sputum positivity was still present. Thus sputum smear examination for AFB should be used for diagnosing all cases of pulmonary tuberculosis. Swaminathan et al<sup>9</sup> found that of the 65 HIV positive cases, who had culture confirmed PTB, 54(83%) were smear positive and 11(17%) were smear negative. Jones and associates<sup>13</sup> in their study reported that positive acid fast smears were present in 30(70%) of 43 patients with < 100 CD4 cells, 17 (85%) of 20 patients with 101 to 200 CD4 cells, 8(50%) of 16 patients with 201 to 300 CD4 cells and 10 (56%) of 18 patients with > 300 CD4 cells. But other studies like Mohanty KC et al<sup>11</sup> in their study reported that only 31.5% of the 57 HIV seropositive patients with tuberculosis had positive sputum smears compared to 73.12% of seronegative patients and Devanayagam CS et al<sup>7</sup> found out of 1600 HIV-TB patients 235(15%) are sputum positive.

Overall sputum positive and sputum negative success rate were 66% and 85%. 29% HIV positive and 1% HIV negative died. But Nimfa M Putong et al<sup>14</sup> – among 271 patients of HIV-TB co-infection 127(47%) lost to follow up, 31(11.4%) successfully treated, 77(28.3%) not successfully treated, 36(13.3%) died.<sup>9</sup> In a study from south India showed cure rate in HIV-TB co-infection was 59-97% and from only TB it was 62-88%. Correlation of CD4 count with treatment response showed CD4 count below 50 had low success rate, i.e. 47% whereas CD4 count above 50 had good response to treatment. Overall change in mean CD4 count was 113 before treatment initiation to 241 after treatment completion. Similar result found in CD4 cell count recovery in HIV-TB co-infection patients by A.Wanchu, VS.Kuttiat, A.Sharma et al<sup>15</sup> in P.G.I Chandigarh- there was a greater improvement in CD4 counts in patients with dual infections taking ATT and ART than without TB taking ART alone, signifying the facts that TB also contributes to decline in the CD4 count in HIV-TB co-infection.

**CONCLUSION:** In our study married males are more commonly affected than females in age group of 25-44 yrs, more frequent in migratory workers; heterosexual route is most common route of transmission. In radiology 55% cases had B/L involvement, 74.5% cases were in moderate to far advanced stage of disease and most common radiological presentation of tuberculosis was parenchymal infiltration(70%) followed by consolidation, cavity, lymphadenopathy, pleural effusion, and miliary shadows. Involvement of lung field in tuberculosis was atypical as evidenced by bilateral lung involvement; middle and lower zone or diffuse involvement. Concomitant EPTB was present in 38% cases(cervical lymph node and pleural effusion 10% each). Most of the patients were in advanced stage of the disease as evidenced by the CD4 count i.e. 92% of the patients had CD4 count < 200. EPTB was most common with CD4 count <100. Smear for sputum AFB was positive in all CD4 ranges, overall positivity was 75%. Treatment outcome was successful in 63% in sputum smear positive cases and 70% in sputum smear negative cases. Treatment outcome was better with CD4 count >50 as compared to CD4 count <50. Hence A strong coordination between the national TB and AIDS control programmes is required for effective management of TB-HIV patients.

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