

## Original Research Article

# Prospective study of tubercular co-infection in HIV infected patients in VIMSAR, Burla, Sambalpur, Odisha, India

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**Received:** 09 April 2018

**Accepted:** 20 April 2018

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### ABSTRACT

**Background:** Tuberculosis is the most common opportunistic infection in HIV positive patient. This is a major challenge faced by HIV positive patient.

**Methods:** This study was carried out at Medicine Department and ART Centre, VIMSAR, Burla to know the epidemiology and clinical profile of HIV and TB co-infection. This is a prospective study in which all adult patients attending to our hospital for period of one year with HIV-TB co infection are enrolled. There were 269 patients. The clinical parameters are studied after all detailed history and clinical examination. The diagnosis of Tuberculosis was made by relevant investigation like Sputum AFB, Chest X-ray, CSF Study, CT Scan, Pleural Fluid Study, Ascitic fluid study etc.

**Results:** The results indicate majority of the patients out of 211 patients 74 (82.52%), were male 34(16.35%) were female and TGTS were-3(1.42%). Age group mostly affected were 26-35 years (38.1%) and 36-45 years (38.1 %). Extra-pulmonary TB constituted 56.28% and Pulmonary TB-43.72%. 41.99% completed anti-TB treatment and mortality was 12.99%. Mean CD4 count at the time of diagnosis-218iu/l; and patients with low CD4 cell count at the time of diagnosis had high mortality.

**Conclusions:** Extra-pulmonary TB is predominant among HIV TB co-infection and the working-class population affected more than the rest TB Meningitis and Disseminated TB are associated with a bad prognosis when compare to other forms of TB. A low CD4 count at the time of Tuberculosis diagnosis is associated with a higher mortality and early suspicion diagnosis of tuberculosis and early initiation of ATT in HIV patients reduces mortality and morbidity significantly.

**Keywords:** AFB, CD4 cell, HIV, NACO, RNTCP, Tuberculosis, WHO, UNAID

### INTRODUCTION

The duo of the two deadly diseases TB and HIV continues to increase morbidity and mortality faced by almost all the physicians of the nation. Resurgence of tuberculosis in western countries due to HIV/AIDS is also being contributing significantly for the disease burden on the globe.

An estimated 1 million people living with HIV (PLHIV) worldwide fell ill with TB in 2016. TB is the leading

cause of death among people with HIV, accounting for some 370,000 people who died from HIV-associated TB in 2016. Globally PLHIV are 20 times (16–27) more likely to fall ill with TB than those without HIV. PLHIV face the threat of drug-resistant TB. If diagnosis is delayed there is increased risk of mortality from multi drug-resistant and extensively drug-resistant TB.<sup>1</sup>

Although curable, tuberculosis is estimated to be the largest cause of death among AIDS patients globally, being, responsible for at least 12% - and perhaps up to 30-

50% - of all AIDS-related deaths that have occurred.<sup>2</sup> At the individual patient level, TB and HIV form a type of "disease complex," with each pathogen manipulating the host response in such a way as to enhance the other pathogen's ability to cause disease pathology. In most cases, mycobacterium is the first pathogen to infect the patient, with HIV infection occurring later.

With progressive HIV infection and its associated with immune compromise state, there is an enhanced risk of reactivation of latent TB infection an increased likelihood of progressive TB disease from newly acquired TB infection, and an increase in recurrent TB or TB relapse. In the cases where HIV infection predates TB infection - such as in mother-to- child transmission of HIV - the generalized immune suppression that accompanies secondary TB infection results in driving HIV replication and disease progression.<sup>3</sup> This study describes the clinical and epidemiological features of HIV-TB co infected patients presented in our hospital.

## METHODS

Patients were enrolled among those attending the General Medicine outdoor and indoor department in respective inpatient wards and ART centre between March 2017 and February 2018. All data were collected from the ART center of VIMSAR, Burla, Sambalpur.

All HIV positive patients were screened for tuberculosis. Those patients with a strong suspicion of HIV/AIDS infection, were subjected to screening tests for anti-HIV antibodies after pre-test counseling and written consent of patient were taken

A detailed clinical history and complete general physical and systemic examination findings of HIV/TB patients were recorded. All the routine investigations were done.

Two simple rapid immune binding assays were selected for the HIV serological testing. It was done in the ICTC center of our institute. The approach was consistent with WHO/NACO recommendations.

The diagnosis of tuberculosis was based on the WHO guidelines case definition of tuberculosis, according to disease type or pulmonary smear status.

All the pulmonary TB suspects were sent to make a sputum smear examination at the RNTCP accredited laboratory in our college. All extra-pulmonary cases were examined individually.

All suspect cases of pulmonary TB gave three sputum specimens to the RNTCP lab. Sputum Negative cases were considered as TB when the chest x ray showed changes consistent with tuberculosis.

## RESULTS

During the period of study 211 patients qualified to be enrolled. 174 (82.52%) were males and 34 (16.35%) were females. 3 were transgender/transsexual.

The age and sex distribution of the patients are shown below in Table 1.

**Table 1: Age and sex distribution.**

Age	Male	Female	Transgender	Total No. of Patients	Percentage (%)
15-25	18	2	-	20	9.95
26-35	64	15	2	81	38.50
36-45	65	14	1	80	38.1
46-55	22	2	-	24	11.26
56-65	3	1	-	4	1.73
>65	2	0	-	2	0.86

Most of the patients were manual labourers (74 =35.06%); followed by unemployed (33=15.58%);(5) Semi skilled worker (26=12.12%); self-employed (21=9.96%); House wife (21=9.96); Local transport worker (12=4.76%); mechanic (3=1.30%); Service (5=2.6%) ; truck driver (21=9.96%); Hotel staff (4=1.73%); Student (4=1.73%); Farmer (3=1.3%); factory worker (2 =0.94%).

The risk for HIV infection by engaging in unsafe sexual practices, such as having multiple sex partners,

unprotected intercourse, sex with high risk partners (e.g. contaminated injectable drug users, commercial sex workers), and exchanging sex for money or drugs.

Most of the patients (206 = 97.84) are heterosexuals while only 4 (1.86%) are homosexuals and all of them were males. Out of the 211 cases 92(43.72%) were Pulmonary tuberculosis and 119(56.28%) were extra-pulmonary tuberculosis. In this study show 119(54.4) EPTB and 92(45.6) PTB, this clearly shows that EPTB is more common than pulmonary TB in HIV- TB co

infection out of 92 patients of PTB 50(54.46) patient were sputum positive for AFB and 42(45.54) were sputum negative.

Pleural effusion (tubercular) (46 = 38.46%) was the most common type of extra-pulmonary TB in our study group. It was followed by lymph node TB (33 = 27.69%) and gastrointestinal TB (19 =16.15%). 11(9.23%) patients had meningeal TB and 5(3.85%) had multiple sites of involvement.

**Table 2: Occupation of patient.**

Occupation	Number	%
Driver	21	9.96
Labourer	74	35.06
Hotel worker	4	1.73
Farmer	3	1.30
House wife	5	2.16
Student	4	1.73
Self-employed	21	9.96
Local transport worker	10	4.76
Service	5	2.60
Semi-skilled worker	26	12.12
Mechanic	3	1.30
Unemployed	33	15.58
Factor workers	2	0.94
Total	100	100

There were 3(1.69%) cases of skin TB and tuberculoma each. 2 cases (1.68%) each of pericardial TB and TB spine were included in the study.

Most of the patients with PTB complained of cough (32=34.78%). Weight loss (18=19.56%) and loss of appetite (20=21.73%) cases. Fever was seen 10 (10.86%) 12 (13.04%) cases had hemoptysis (5).

**Table 3: Mode of transmission.**

Mode of transmission	No.	Percentage
Heterosexual contact	206	97.39
Blood transfusion	1	0.37
Injectable drug abuse	1	0.37
Homosexual	4	1.85

Most of the patients with EPTB had fever 8 (6.72%), weight loss 10 (8.40%) and loss of appetite 7 (5.88%). Abdominal distension 7 (5.88%) and diarrhea 8 (6.72%)

**Table No.4: Extra Pulmonary Tuberculosis manifestation.**

TB	Pleural	Pericardial	CNS	Abdominal	Bone and	Skin TB	Tuberculoma
Lymphadenitis	Effusion	Effusion	(TBM)	TB	Joint TB		
33 (27.69%)	46 (38.46%)	2 (0.99%)	5(0.3.85%)	19(16.15%)	2(0.99%)	3(1.54%)	3

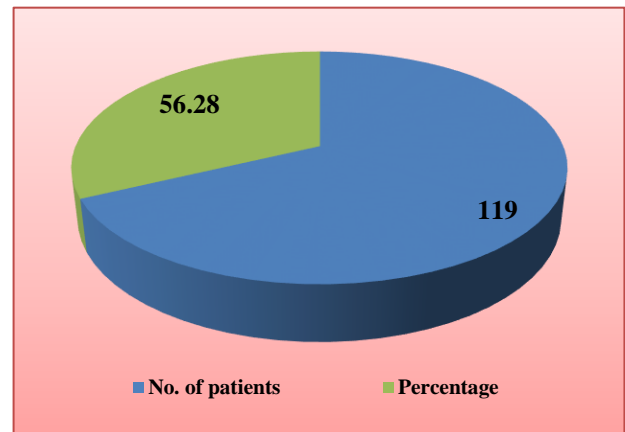
were the major symptoms in gastrointestinal TB, while cough 28 (23.52%) and chest pain 6 (5.04%) were the major symptoms in pleural TB.

Neck was the commonest site for TB lymphadenitis 18 (15.12%) cases, Fatigue 1 (0.84%) cases. Most, of the patients with TB meningitis presented with altered sensorium 1 (0.84%).

Out of the 92 cases of PTB in our study, 47(51.49%) patients had infiltrations in upper zone in chest x-ray. 19 (20.79%) had fluffy shadows and 10 (10.89%) had non-homogenous patches.

Miliary shadows were present in 9(9.9%) cases. 4(3.96%) cases had consolidation and 2(1.98%) had cavity. One (0.99%) chest x-ray had bronchiectasis changes and another one had an isodense shadow.

In our study, 45 (21.21 patients were having a CD4 cell count, between 51-100 at the time of diagnosis of TB 37 (7.75) were in the 101-150 group and 30 (14.29) patient in the 151-200 group. 17(8.23%) patients had less than 50 CD4 cells/ mm<sup>3</sup>.



**Figure 1: Chart showing types of tuberculosis.**

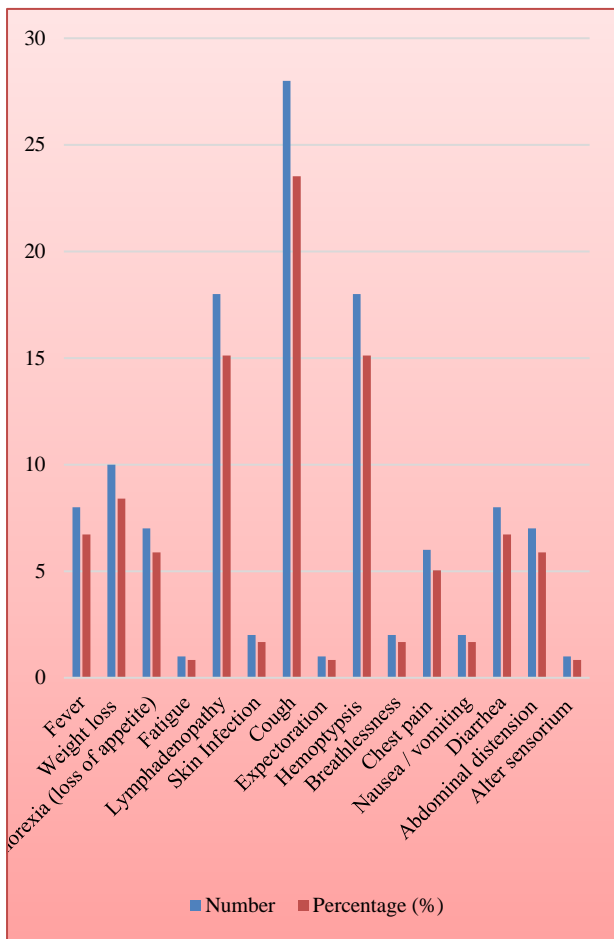
Another two groups of 17(8.23%) patients each had CD4 cell count between 210-250 and 301-350. 14(6.93%) patients had CD4 cell count more than 500. 14(6.49%) had it between 251-300, 8(3.9%) between 401-450, 7(3.03%) between 351-400 and 4(1.73%) between 451-500.

The mean CD4 count of patients having HIV-TB co-infection was 218 cells/mm<sup>3</sup>.

Majority of the patients 181 (86.24%) were started on CAT 1 ATT. 19 (9.29%) patients had CAT 2ATT. 2(1.3%) patients were having MDR TB.3(3.46%) patients had taken non-DOTS therapy.

**Table 5: Clinical findings in Pulmonary TB**

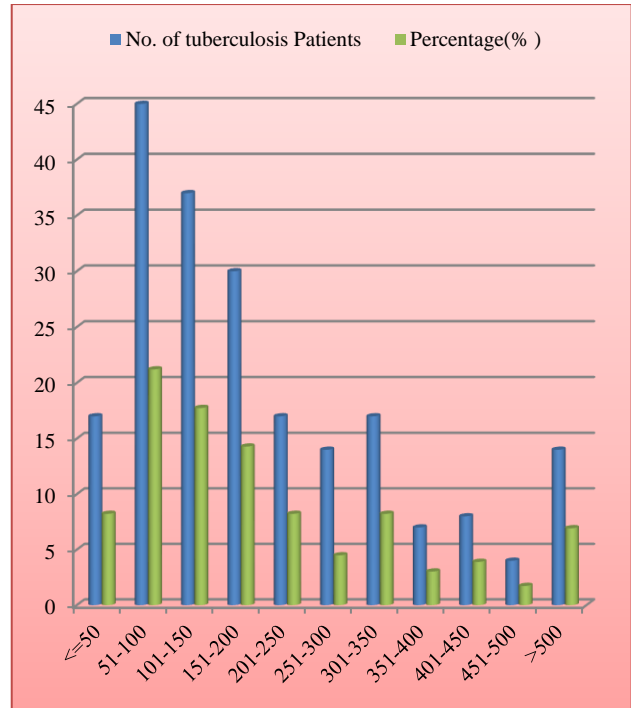
Types of symptoms	Number	%
Fever	10	10.86
Weight loss	18	19.56
Anorexia (loss of appetite)	20	21.73
Lymphadenopathy	-	-
Cough	32	34.78
Expectoration	1	1.08
Hemoptysis	12	13.04



**Figure 2: Clinical finding in Extra Pulmonary TB.**

**Table 6: Chest X-ray findings**

X-ray findings	No. of patients	%
Upper zone infiltration	47	51.49
Fibro-cavity lesion	2	1.98
Military shadow	9	9.9
Homogenous patches	10	10.89
Consolidation	4	3.96
Fluffy shadow	19	20.79



**Figure 3: CD4 cell count**

**DISCUSSION**

This study which was carried out for a period of one year revealed that the disease burden of tuberculosis is substantial among the HIV affected population. Tuberculosis still marks as the leading cause of mortality and morbidity among the PLHA patients. Total number of patients enrolled in our study was 211 which included all the patients who came to the ART centre of our hospital and the general medicine wards for a period of one year. During the same period of time 269 new cases of HIV were registered in the ART centre and department of medicine of our institute. Among them 211 individuals contracted tuberculosis during the study period.

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. The Studies showed a clear male majority in HIV-TB co-infection.<sup>4</sup> The studies in Manipur and Iran also showed that males are more affected than female.<sup>5,6</sup> But a study in Mumbai showed a marginal female majority as large number of female sex workers were included in that study.<sup>7</sup>

The high prevalence of HIV in males in our study must be due to the high rate of migration of the youth to other states in search of job opportunities where they are exposed to high risk activities. The main regions of migration include Surat in Gujarat, Mumbai, Chennai and Kerala.<sup>8</sup> Another reason for the large male to female disparity may be because the females are often neglected and deprived of health care facilities resulting in an underestimation of their numbers.

The mean age of patients in our study was 37 years and the range was from 15 years to 70 years. The major age groups were 26-35 and 36-45 years which comprised of 76:6% (38.5% and 38.1%) of the study population. This clearly shows that the working population of the society is affected more than the rest as they are more sexually active and also have more chances for exposure to TB infection. This is consistent with the studies reported that 26 patients, (11.26%) were between 46-55 years and 23(9.95%) were between 15 and 25 years.<sup>7</sup> Only four patients were above 56 years of age. The decrease in number of elderly population is may be due to the high mortality of the HIV patients in the region. Majority of the participants are manual labourers (74 =35.06%) working either in their native place or in the above mentioned high risk migrant areas. This is consistent with the study in Delhi which had 38.5 % of manual labourers.<sup>9</sup> The dwelling areas of the labourers are congested and are often deprived of adequate ventilation or hygiene which make them prone to infections especially tuberculosis.<sup>10</sup> 162 (77.06%) of the patients were married while 29 (13.85%) were unmarried. This is contrary to many other studies especially those done outside India and may be due to the social & cultural difference. 19 (9.09%) patients were single due to various reasons like death of the partner, divorce etc. The affected husbands are the viral source for most of village women.<sup>11</sup> Out of the 211 patients with HIV-TB co-infection include 92 (43.72%) patients suffered from Pulmonary TB. The rest 119 patients were diagnosed to have extra pulmonary TB (56.28%). This clearly show that EPTB is more common than pulmonary TB in HIV. TB co-infection similar to our study.<sup>9</sup>

A study in Thailand had 70% pulmonary and 30% extra pulmonary TB due to advance immune suppression<sup>12</sup> out of 92 patients of PTB 50(54.46%) patients were sputum positive for AFB and 42(45.54) were sputum negative. in several studies have found smear negative is more common among HIV TB patients.<sup>12,13</sup> The relationship between CD4 count and Tuberculosis considered very important as the decline in the level immunity is considered as a major risk for acquisition and reactivation of infections. It ranged from 21-1044 cells/mm. It is slightly higher than what had derived from his studies (mean=174).<sup>14</sup> It was even less the study done in Shimla (mean= 123) and a study in AIIMS, New Delhi reported (mean CD4 count= 120).<sup>15,16</sup> But in a study the CD4 counts were better than ours (mean = 307; range = 6-1531).<sup>17</sup>

Out of the 92 cases of PTB in our study, 47 (51.49%) patients had infiltrations in upper zone in chest x-ray. 19 (20.79%) had fluffy shadows and 10 (10.89%) had nonhomogenous patches. Miliary shadows were present in 9(9.9%) cases. 4 (3.96%) cases had consolidation and 2(1.98%) had cavity. One (0.99%) cases chest x-ray had bronchiectasis changes and another one had an isodense shadow in contrast mid zone/lower zone shadow 8

(22.9%) cases. unifocal alveolar opacity in 7 (20%) cases. Pleural effusion 5 (14.3%) cases.<sup>18</sup>

This study concluded that in the selected population the risk of Tuberculosis increases remarkably when the CD4 count falls below 200 cells/mm. (61.5% of the patients had a CD4 count  $\leq$ 200). The highest number of TB cases were recorded when the CD4 count was between 51 to 100 (21.21 %). Though there is a decline in the number of cases as the CD4 count increases, TB is prevalent in all groups. In the study reported, 78.4% of patients of HIV-TB co-infection were having CD4 count  $\leq$ 200cells/mm). The study reported 81.6% of patients with CD4 count less than 200cells/mm<sup>3</sup>(23) This contrary data suggest that our study population acquire TB infection even if the CD4 count higher may be because of higher prevalence of TB in general population in this part of the state. Our study reported that in the selected population the risk of Tuberculosis increases remarkably when the CD4 count falls below 200 cells/mm. (61.5% of the patients had a CD4 count  $\leq$ 200). The highest number of TB cases were recorded when the CD4 count was between 51 to 100 cell/mm (21.21 %). Though there is a decline in the number of cases as the CD4 count increases, TB is prevalent in all groups as reported, 78.4% of patients of HIV-TB co-infection were having CD4 count  $\leq$ 200cells/mm<sup>3</sup> and. 81.6% of patients with CD4 count less than 200cells/mm<sup>3</sup>. This contrary data suggest that our study population acquire TB infection even if the CD4 count higher may be because of higher prevalence of TB in general population in this part of the state.<sup>15</sup>

Majority of the patients (181= 86.24%) were started on therapy CAT 1 ATT. 9(9.09%) patients had CAT 2 ATT. 2(1.3%) patients were having MDR TB. 7(3.46%) patients had taken non-DOTS therapy. Out of the 211 patients in our study 89(41.99%) were declared TB cured after treatment. Another 89(41.99%) patients are continuing the treatment. 27(12.99%) patients died and 6 (3.03%) were lost to follow up. This is compared with study in Karnataka with a cure rate of 75.6%; death- 11.78%; lost follow up - 3.12% and 9.49% of patients continuing treatment.<sup>20</sup> Low number of cured patients in our study may be because of the large number of patients continuing the treatment. The study had reported death rate of 15.7%.<sup>21</sup>

## CONCLUSION

HIV- TB co infection is a major challenge in healthcare system globally. It most commonly affects the younger economically productive and sexually active section of the society. Early suspicion diagnosis and early initiation of ATT in HIV-TB patients reduces mortality and morbidity significantly. CD4 cell count were inversely related to Tubercular infection in HIV patients. Decrease in CD4 cell count increase in Tubercular infection. Male are commonly affected in compare to female. Extra-pulmonary tuberculosis is common in compare to Pulmonary Tuberculosis. Therefore, adequate knowledge



of the manifestations of tuberculosis in HIV-infected patients is absolutely necessary for optimal management and to reduce mortality and morbidity.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Bariha PK, Pujari UP, Kullu BK, Thakur A. Prospective study of tubercular co-infection in HIV infected patients in VIMSAR, Burla, Sambalpur, Odisha, India. *Int J Adv Med* 2018;5:530-5.