### **ORIGINAL ARTICLE**

## TUBERCULOSIS IN PATIENTS LIVING WITH HIV/AIDS: TYPES AND ITS RELATION TO CD4 COUNT

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#### ABSTRACT

**Introduction:** TB is the most common opportunistic infection and a leading killer of people living with HIV/AIDS (PLWHA). HIV not only increases the number of TB cases, but also alters the clinical course of TB disease. As HIV related immunosuppression increases, the clinical pattern of TB changes, with increasing numbers of smear-negative and extrapulmonary cases.

**Methodology:** Total 100 HIV positive patients diagnosed with Tuberculosis and having age more than or equal to 18 years were selected randomly from the list obtained from ART centre using random number table. Detailed clinical and laboratory investigations were done in all patients.

**Results:** Common presenting symptom in this study was fever (91%), cough (65%), anorexia (62%), weight loss (61%), diarrhea (58%) and breathlessness (36%). Out of total 100 study participants, 54 were having pulmonary tuberculosis and 46 were having extrapulmonary tuberculosis. In extrapulmonary TB Spleen (41%) was most commonly involved followed by Lymphnode (39%), pleural effusion (12%) and meningitis (8%). Among pulmonary TB patients maximum number of patients 24 (44.44%) were having CD4 count 100 - 199 per mm<sup>3</sup>. Among Extrapulmonary TB patients, maximum number of patients 28 (60.87%) were having CD4 count 100 -199 per mm<sup>3</sup>.

**Conclusion**: The presenting symptoms of tuberculosis in PLHIVs were not different from those of non HIV patients. Generally patients with low CD4 count presents with atypical form of tuberculosis.

Keywords: PLHIV, Extrapulmonary TB, CD4 count

#### INTRODUCTION

TB is the most common opportunistic infection and a leading killer of people living with HIV/AIDS (PLWHA), killing 1 of 3 patients.<sup>1</sup> The risk of developing tuberculosis (TB) is estimated to be between 26 and 31 times greater in people living with HIV (PLHIV) than among those without HIV infection. In 2013, there were 9 million new cases of TB, of which 1.1 million were among people living with HIV in the world.<sup>2</sup>

With HIV pitching in, TB incidence levels could go up close to 2.0 million or more per year in India, assuming HIV rates close to 1 percent and the incidence of TB remaining at 1990 levels. Therefore, the task of controlling the dual epidemic of TB and HIV/AIDS remains a major challenge for the country.

HIV fuels the TB epidemic in several ways. HIV promotes the progression to active TB disease, both in people with recently acquired TB infection

and with latent *M. tuberculosis* infection. HIV is the most powerful risk factor for reactivation of latent tuberculosis infection to active disease. HIV infected persons are more susceptible to becoming infected with TB when exposed to *M. tuberculosis*. HIV increases the rate of recurrent TB disease, which may be due to either endogenous reactivation (true relapse) or exogenous re-infection.<sup>3</sup>

HIV not only increases the number of TB cases, but also alters the clinical course of TB disease. As HIV related immunosuppression increases, the clinical pattern of TB changes, with increasing numbers of smear-negative and extrapulmonary cases. In addition, TB disease is more likely to be disseminated and more difficult to diagnose as the immunosuppression progresses. HIV infected TB patients can also suffer from other HIV related diseases. National TB programmes in the high HIV burden countries are reporting increasing case fatality rates of up to 25 percent in the smearpositive and 40-50 percent in smear-negative pulmonary TB patients.<sup>4</sup>

Rates of smear-negative pulmonary and extrapulmonary tuberculosis have been rising in countries with HIV epidemics. The mortality rate among HIV-infected tuberculosis patients is higher than that of noninfected tuberculosis patients, particularly for those with smear-negative pulmonary and extrapulmonary tuberculosis. Delayed diagnosis may be an important cause of excess mortality in people living with HIV who have smear-negative pulmonary and extrapulmonary tuberculosis.<sup>5</sup>

The guideline of the World Health Organization to initiate HAART at CD4 T-cell count  $\leq 350/\mu L$  should therefore be followed strictly to prevent TB or other opportunistic infections.<sup>6</sup>

The unprecedented scale of the HIV-related TB epidemic demands urgent, effective and coordinated action to improve diagnostic, care and prevention services for people living with HIV and TB. However, this does not require the development of an independent programme for TB/HIV but simply closer collaboration between existing TB and HIV control programmes to exploit synergies, avoid overlaps and fill the gaps in service provision.<sup>7</sup>

The current study is therefore aimed at finding types of TB among PLHIVs and the relation of different type of TB to CD4 count of the patients.

#### METHODOLOGY

This study was conducted in a tertiary care hospital of Surat, Gujarat, India. Total 100 HIV positive patients diagnosed with Tuberculosis and having age more than or equal to 18 years were selected randomly from the list obtained from ART centre using random number table. TB-HIV patients having age less than 18 years were excluded from the study.

Patients were contacted during their routine visit to ART centre. Informed written consent was obtained from all patients after explaining them nature of the study. All patients those cannot be traced or refused to participate in the study were excluded and immediate next patient from the list was recruited in the study.

Permission from Institutional Ethical Committee was obtained.

In all eligible patients, following data was recorded.

- Detailed history regarding the mode of onset of the disease, clinical profile and duration.
- Detailed past and family history.
- Detailed general and systemic examination
- Routine investigations HB with ESR, Total and differential count, Urine routine and micro
- Specific investigations Chest X-ray, CD 4 Count, Ultrasonography
- Lymphnode FNAC, Pleural fluid analysis, Ascitic fluid analysis, CT scan/MRI – whenever indicated

All data were entered in the epi-info software and data analysis was carried out.

#### RESULT

Total 100 HIV positive patients diagnosed with Tuberculosis were recruited in the study. Out of these, 80% were male and 20% were female. Most common presenting symptom in tuberculosis patients was fever (91%) and cough (65%). Anorexia, weight loss and diarrhea was presenting complain in 60 to 65% of patients. Serious symptoms like hemoptysis, convulsion and altered consciousness was presenting complaint in 15%, 11% and 5% of patients respectively.

Table 1: Distribution of patients according to their presenting symptoms (n=100)

Symptom	Patients
Fever	91
Cough	65
Anorexia	62
Weight Loss	61
Diarrhoea	58
Breathlessness	36
Headache	25
Lymphadenopathy	15
Hemoptysis	15
Chest Pain	11
Convulsion	11
Altered Consciousness	5

# Table 2: Distribution of patients according to type of tuberculosis (n=100)

Type of TB	Cases (%)
Pulmonary TB	54 (54)
Extrapulmonary TB	46 (46)
Both	6 (6)

Out of total 100 study participants, 54 were having pulmonary tuberculosis and 46 were having extra-

pulmonary tuberculosis. 6 patients were having both pulmonary and extrapulmonary tuberculosis.

Table 3: Distribution of Extrapulmonary TB patients according to its type (n=46)

Type of Extrapulmonary TB	Cases (%)
Splenic TB	19 (41.30)
TB Lymphadenitis	18 (39.13)
Pleural Effusion	12 (26.09)
Meningitis	8 (17.39)
Miliary TB	1 (2.17)
Ascitis	1 (2.17)

Table 3 shows the distribution of total 46 patients diagnosed with extrapulmonary TB patients according to its type. Table shows that Splenic Tuberculosis (41.30%) was the most common among the extrapulmonary TB cases. 39.13% cases were of TB Lymphadenitis. Pleural effusion contributes to 12 (26.09%) cases.

Table 4: Distribution of patients according toCD4 count and type of Tuberculosis

CD4+ T cell count	Pulmonary TB (%) (n=54)	Extrapulmonary TB (%) (n=46)
> 500	3 (5.56)	0 (0.0)
200 - 499	12 (22.22)	11 (23.91)
100 - 199	24 (44.44)	28 (60.87)
< 100	15 (27.78)	7 (15.22)

Table 4 shows CD4 count and type of TB among patient of TB. Among pulmonary TB patients maximum number of patients 24 (44.44%) were having CD4 count between 100-199 per mm<sup>3</sup>. Among Extrapulmonary TB patients, maximum number of patients 28 (60.87%) were having CD4 count between 100-199 per mm<sup>3</sup>. Only 3 (5.56%) patients of pulmonary TB were having CD4 count more than 500 per mm<sup>3</sup>. Among extrapulmonary TB patients, no patients were having CD4 count more than 500 per mm<sup>3</sup>.

#### DISCUSSION

In present study 100 HIV positive patients with tuberculosis were studied. Male to female ratio in present study was found 4:1. This was similar to findings of Zuber et al who reported male:female ration of around 4.8:1.<sup>8</sup>

Common presenting symptom in this study was fever (91%), cough (65%), anorexia (62%), weight loss (61%), diarrhea (58%) and breathlessness (36%). Zuber et al study also shows most common

In present study pulmonary tuberculosis with both typical and atypical presentation was the most common manifestation of TB (54%) while extrapulmonary TB in which lymphatic system (37%) was most commonly involved followed by pleural effusion meningitis (12%)and (8%).Our study correlates with study done by Zuber et al. in which pulmonary TB was the most common manifestation of TB (80%), and also suggested a high extrapulmonary involvement (38.46%) patients. Lymphatic system was most commonly involved in 18% followed by pleural involvement in 14% cases.8

Lymph node TB (LNTB) is the commonest form of Extra Pulmonary TB (EPTB). Most studies in peripheral LNTB have described a female preponderance, while pulmonary TB is more common in adult males. In the era before the HIV pandemic, and in studies involving immunocompetent adults, it was observed that EPTB constituted about 15 to 20 percent of all cases of TB in general practice. HIV infected persons are at markedly increased risk for primary or reactivation TB and for second episodes of TB from exogenous re-infection. In some settings, EPTB can account for up to 53 to 62 percent of cases of TB in HIV-positive individuals.<sup>9, 10, 11</sup>

Rates of smear-negative pulmonary and extrapulmonary tuberculosis have been rising in countries with HIV epidemics. The mortality rate among HIV-infected tuberculosis patients is higher than that of noninfected tuberculosis patients, particularly for those with smear-negative pulmonary and extrapulmonary tuberculosis. Delayed diagnosis may be an important cause of excess mortality in people living with HIV who have smear-negative pulmonary and extrapulmonary tuberculosis.<sup>5</sup>

The clinical manifestation of TB in HIV-infected patients was quite varied and generally shows different patterns as CD4 count. In patient with relatively high CD4 count, the typical of pulmonary reactivation occurs, while in patients with lower CD4 count disseminated disease was more common.

This finding was similar to Bishnu Et al who documented lower CD4 count was strongly associated with the higher odds of PTB.<sup>12</sup>

This finding suggests the extent of missed opportunity of preventing TB, probably due to a delayed start of HAART; earlier initiation, may have a significant effect on reducing the incidence of TB. Lower CD4 count is a well-established risk factor for development of active TB among HIV-infected people.<sup>13, 14</sup>

#### CONCLUSION

Proportion of male patient was high among PLHIV TB patients. Most common presenting complain was fever followed by cough, anorexia, weight loss and diarrhoea. Thus, the presenting symptoms of tuberculosis in PLHIVs were not different from those of non HIV patients. Generally patients with low CD4 count presents with atypical form of tuberculosis.

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